**Online Data Supplement**

**Title:** Does Obesity Protect Against Death in Sepsis? A Retrospective Cohort Study of 55,038 Adult Patients

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**eAppendix 1. Adapted Electronic Health Record SOFA Score**

This is an overview of how the SOFA scores were implemented in the Cerner HealthFacts Dataset. The primary goal was to use daily SOFA scores to implement EHR versions of the SCCM/ESICM Sepsis-3 Definition (which is defined as suspected infection with a concurrent rise in SOFA score by >=2). Secondarily, SOFA scores were used for severity-of-illness characterizations and adjustments.

The tables below show the SOFA score and the adapted EHR version. Note that the SOFA score for Hepatic (bilirubin) and Coagulation (platelets) systems are unchanged, while the Renal adaptation simply removes the urine output component because urine output data is not available. The Cardiovascular criteria was adapted because vasopressor doses are unavailable. The Pulmonary criteria were adapted based on studies by Bilan and colleagues and Rice and colleagues which found that SaO2/FiO2 ratios correlated and had acceptable sensitivities and specificities for PaO2/FiO2 ratios. Lastly, the Neurologic criteria may need to be ignored (note that there is some precedent for doing this in the literature).

**Infection Present-On-Admission** (blood culture or first antibiotic on hospital day 1 or 2) - the baseline SOFA score was defined as the lowest SOFA score during hospitalization for patients with infection present-on-admission reasoning that most patients that survive a hospitalization have a return in their organ function to close to their healthy state prior to discharge.  However, the baseline SOFA score only incorporated the neurologic, renal, hepatic, and coagulation components of the SOFA score; thus, any cardiovascular or respiratory SOFA points were always counted as “new” (since hypotension and hypoxemia typically indicate an acute process, whereas dementia, kidney or hepatic disease, or thrombocytopenia are often chronic).  For patients that died or were discharged to hospice within 3 days of hospital admission, however, the baseline SOFA score was considered to be zero (since these patients would not return to their normal “healthy” state of organ function).

**Hospital-Onset Infection** (blood culture day and first antibiotic on or after calendar day 3) - the baseline SOFA score was defined as the lowest SOFA score in the 7 days prior to the blood culture day.

**Table 1. SOFA Score.**

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| --- | --- |
| Organ System | **SOFA Score** |
| Neuro | 1 - GCS score 13-14  2 - GCS score 10-12  3 - GCS score 6-9  4 - GCS score <6 |
| Cardiovascular | 1 – MAP (Mean Arterial Pressure) <70 mmHg  2 - Dopamine ≤ 5 mcg/kg/min or Dobutamine (any dose)  3 - Dopamine > 5 mcg/kg/min or Epinephrine ≤0.1 mcg/kg/min or Norepinephrine ≤0.1 mcg/kg/min  4 - Dopamine > 15 mcg/kg/min or Epinephrine >0.1 mcg/kg/min or Norepinephrine >0.1 mcg/kg/min |
| Pulmonary | 1 - PaO2/FiO2 ratio 300-399  2 - PaO2/FiO2 ratio 200-299  3 - PaO2/FiO2 ratio 100-199 and mechanically ventilated  4 - PaO2/FiO2 ratio <100 and mechanically ventilated |
| Renal | 1 - Creatinine 1.2-1.9  2 - Creatinine 2.0 – 3.4  3 - Creatinine 3.5 – 4.9 or urine output <500 cc/day  4 - Creatinine >5.0 or urine output <200 cc/day |
| Hepatic | 1 - Bilirubin 1.2-1.9  2 - Bilirubin 2.0 – 5.9  3 - Bilirubin 6.0 – 11.9  4 - Bilirubin >12.0 |
| Coagulation | 1 - Platelets <150  2 - Platelets <100  3 - Platelets <50  4 - Platelets <20 |

**Table 2. Adapted EHR SOFA Score.**

|  |  |
| --- | --- |
| Organ System | **Adapted Version** |
| Neuro | 1 - GCS score 13-14  2 - GCS score 10-12  3 - GCS score 6-9  4 - GCS score <6 |
| Cardiovascular | 0 – MAP (Mean Arterial Pressure) >= 70 mmHg  1 – MAP (Mean Arterial Pressure) <70 mmHg  2 – Any dopamine, dobutamine, or phenylephrine  3 – Any norepinephrine or epinephrine  4 – Any two “concurrent” (on the same day) vasopressors (norepinephrine, epinephrine, vasopressin, phenylephrine, or dopamine) |
| Pulmonary | 0 – PaO2/FiO2 ratio >=400, or SaO2/FiO2 ratio >301  1 – PaO2/FiO2 ratio 300- <400, or SaO2/FiO2 ratio 221-301  2 – PaO2/FiO2 ratio <300 or SaO2/FiO2 ratio <221  3 – PaO2/FiO2 ratio 100- <200 (or SaO2/FiO2 ratio 67 -141) AND ICD-9 or CPT code for mechanical ventilation  4 – PaO2/FiO2 ratio <100 (or SaO2/FiO2 ratio <67) AND ICD-9 or CPT code for mechanical ventilation |
| Renal | 0 – Creatinine <1.2  1 - Creatinine 1.2-<2.0  2 - Creatinine 2.0 – <3.5  3 - Creatinine 3.5 – <5.0 (urine output removed)  4 - Creatinine >=5.0 (urine output removed) |
| Hepatic | 0 – Bilirubin < 1.2  1 - Bilirubin 1.2- <2.0  2 - Bilirubin 2.0 – <6.0  3 - Bilirubin 6.0 – <12.0  4 - Bilirubin >=12.0 |
| Coagulation | 0 – Platelets >=150  1 - Platelets 100- <150  2 - Platelets 50-<100  3 - Platelets 20-<50  4 - Platelets <20 |

* Bilan N, Dastranji A, Ghalehgolab Behbahani A. Comparison of the spo2/fio2 ratio and the pao2/fio2 ratio in patients with acute lung injury or acute respiratory distress syndrome. J Cardiovasc Thorac Res. 2015;7(1):28-31
* Rice TW, Wheeler AP, Bernard GR, Hayden DL, Schoenfeld DA, Ware LB; Comparison of the SpO2/FIO2 ratio and the PaO2/FIO2 ratio in patients with acute lung injury or ARDS. Chest. 2007 Aug;132(2):410-7.
* Singer  M, Deutschman  CS, Seymour  CW,  et al.  The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3).  JAMA. 2016;315(8):801-810.
* Seymour  CW, Liu  VX, Iwashyna  TJ,  et al.  Assessment of clinical criteria for sepsis: for the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3).  JAMA. 2016;315(8):762-774.
* Vincent  JL, Moreno  R, Takala  J,  et al; Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine.  The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure.  Intensive Care Med. 1996;22(7):707-710.

**eAppendix 2. Medications Used in Study (Antibiotics and Vasopressors)**

For purposes of case-finding criteria, the antibiotics were divided into parenteral (IV) and oral (PO) antibiotics. “Antibiotics” include antibacterial, antifungal, and antiviral agents. All PO and IV antibiotics were considered identical for purposes of determining whether an antibiotic is “new” or not (meaning that a switch from IV to PO or vice versa does not count as a “new antibiotic.”) The one exception is IV vs PO Vancomycin (meaning that a switch from IV to PO vancomycin, or initiation of PO vancomycin while still on IV vancomycin, and vice versa, all count as “new” antibiotics). Intramuscular (IM) antibiotics were treated equivalently as IV antibiotics. The generic names of the antimicrobials included are listed below.

|  |
| --- |
| **ANTIBIOTICS** |
| *IV Antibacterials* |
| amikacin, ampicillin, ampicillin/sulbactam, azithromycin, aztreonam, cefamandole, cefazolin, cefepime, cefmetazole, cefonicid, cefoperazone, cefotaxime, cefotetan, cefoxitin, ceftaroline, ceftazidime, ceftazidime/avibactam, ceftizoxime, ceftolozane/tazobactam, ceftriaxone, cefuroxime, cephalothin, cephapirin, chloramphenicol, ciprofloxacin, clindamycin, cloxacillin, colistin, dalbavancin, daptomycin, doripenem, doxycycline, ertapenem, gatifloxacin, gentamicin, imipenem, kanamycin, levofloxacin, lincomycin, linezolid, meropenem, methicillin, metronidazole, mezlocillin, minocycline, moxifloxacin, nafcillin, oritavancin, oxacillin, penicillin, piperacillin, pileracillin/tazobactam, polymyxin B, quinupristin/dalfopristin, streptomycin, tedizolid, telavancin, ticarcillin, ticarcillin/clavulanate, tigecycline, tobramycin, trimethoprim/sulfamethoxazole, vancomycin |
| *PO Antibacterials* |
| amoxicillin/clavulanate, amoxicillin, ampicillin, azithromycin, cefaclor, cefadroxil, cefdinir, cefditoren, cefixime, cefpodoxime, cefprozil, ceftibuten, cefuroxime, cephalexin, cephradine, chloramphenicol, cinoxacin, ciprofloxacin, clarithromycin, clindamycin, cloxacillin, dicloxacillin, doxycycline, fidaxomicin, fosfomycin, gatifloxacin, levofloxacin, lincomycin, linezolid, metronidazole, minocycline, moxifloxacin, nitrofurantoin, norfloxacin, ofloxacin, penicillin, pivampicillin, rifampin, sulfadiazine, sulfadiazine-trimethoprim, sulfamethoxazole, sulfisoxazole, tedizolid, telithromycin, tetracycline, trimethoprim, trimethoprim-sulfamethoxazole, vancomycin |
| *IV Antifungals* |
| amphotericin B, anidulafungin, caspofungin, fluconazole, itraconazole, micafungin, posaconazole, voriconazole |
| *PO Antifungals* |
| fluconazole, itraconazole, posaconazole, voriconazole |
| *IV Antivirals* |
| acyclovir, ganciclovir, cidofovir, foscarnet, peramivir |
| *PO Antivirals* |
| Oseltamivir |

The five vasopressors of interest were Norepinephrine, Epinephrine, Dopamine, Vasopressin, and Phenylephrine. We only included intravenous administrations of vasopressors, and excluded vasopressors that were clearly single bolus injections rather than continuous vasopressor infusions.

**eAppendix 3. Definitions of Blood Cultures and Clinical Cultures**

For the primary EHR surveillance definition, blood cultures were used as the center of the surveillance window (regardless of blood culture results). We included bacterial (aerobic and/or anaerobic), acid-fast bacilli (AFB), and fungal blood cultures. Blood cultures for specific viruses (e.g., cytomegalovirus) were excluded.

|  |
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| TESTS INCLUDED AS “CLINICAL CULTURES” |
| Bacterial, fungal, or acid-fast bacilli cultures from the following sites: blood, urine, respiratory, cerebrospinal fluid, pleural, peritoneal, joint/synovial, abscess, wound, sinus, drain, catheter tip, medical devices, stool |
| Respiratory viral tests (rapid antigen, direct fluorescent antibody, polymerase chain reaction): influenza, parainfluenza, respiratory syncytial virus, adenovirus, metapneumovirus |
| Clostridium difficile toxin assays (ELISA or polymerase chain reaction) |
| Specific organism antigens from serum, urine, or cerebrospinal fluid, such as: Cryptococcus, Histoplasma, *Haemophilus influenza*, *Streptococcus pneumoniae*, *Legionella pneumophila* |
| Specific organism cultures or smears, such as: Pneumocystis, Nocardia, Legionella, Malaria |
| *Notable microbiology tests that were not included: Surveillance cultures (e.g., MRSA, VRE), tests for sexually transmitted diseases, HIV tests, parasite tests, H. pylori, Hepatitis, Fungal markers (galactomannan, beta-D-glucan), serological tests (IgM, IgG), Gram stains alone without a culture, non-respiratory viral cultures or PCRs (e.g., CMV)* |

Growth of any organism from a blood culture was considered to be positive, with the exception of the following common skin contaminants:

• Coagulase negative Staphylococci

• Bacillus species not anthracis

• Corynebacterium species

• Aerococcus species

• Micrococcus species

• Propionibacterium species

**eAppendix 4. Volume of sepsis admissions**

We used each hospital’s sepsis rate to determine its volume of sepsis admissions. The hospital sepsis rate was expressed as a percentage (100 times the mean annual volume of sepsis/ mean annual volume of adult admissions). This hospital sepsis rate was expressed in three strata: low, medium or high (i.e., volume of sepsis admissions).

**eAppendix 5. Site of infection**

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| **Source of Infection** | **ICD-9-CM Codes** |
| Urinary tract infection | 095.4, 099.4, 590, 595.0, 597, 598.0, 599.0 |
| Pneumonia | 032.0–032.3, 034.0, 098.6, 101, 460–465, 473.0–474.0, 475, 022.1, 031.0, 033, 095.1, 466, 480–487, 510, 511.1, 513, 517.1, 770.0 |
| Intra-abdominal | 001–009, 022.2, 095.2, 098.7, 540–542, 566, 567.0–567.2, 569.5, 070, 095.3, 573.1, 573.2, 576.1 |
| Skin and Soft Tissue | 680–686 |
| Septicemia/ bacteremia | 038.9, 790.7 |
| Multiple | More than one condition e.g. urinary tract infection and pneumonia |
| Other site specified/unspecified | All cases not classified by above codes |

Christensen KL, Holman RC, Steiner CA, Sejvar JJ, Stoll BJ, Schonberger LB. Infectious disease hospitalizations in the United States. Clin Infect Dis. 2009 Oct 1;49(7):1025-35

|  |  |
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| **eAppendix 6. Enhanced ICD-9-CM Coding Algorithms for Elixhauser Comorbidities** \* | |
| **Comorbidities** | **Enhanced ICD-9-CM** † |
| Congestive heart failure | 398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4–425.9, 428.x |
| Cardiac arrhythmias | 426.0, 426.13, 426.7, 426.9, 426.10, 426.12, 427.0–427.4, 427.6–427.9, 785.0, 996.01, 996.04, V45.0, V53.3 |
| Valvular disease | 093.2, 394.x–397.x, 424.x, 746.3–746.6, V42.2, V43.3 |
| Pulmonary circulation disorders | 415.0, 415.1, 416.x, 417.0, 417.8, 417.9 |
| Peripheral vascular disorders | 093.0, 437.3, 440.x, 441.x, 443.1– 443.9, 447.1, 557.1, 557.9, V43.4 |
| Hypertension, uncomplicated | 401.x |
| Hypertension, complicated | 402.x–405.x |
| Paralysis | 334.1, 342.x, 343.x, 344.0–344.6, 344.9 |
| Other neurological disorders | 331.9, 332.0, 332.1, 333.4, 333.5, 333.92, 334.x–335.x,  336.2, 340.x, 341.x, 345.x, 348.1, 348.3, 780.3, 784.3 |
| Chronic pulmonary disease | 416.8, 416.9, 490.x –505.x, 506.4, 508.1, 508.8 |
| Diabetes, uncomplicated | 250.0–250.3 |
| Diabetes, complicated | 250.4–250.9 |
| Hypothyroidism | 240.9, 243.x, 244.x, 246.1, 246.8 |
| Renal failure | 403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 585.x, 586.x, 588.0, V42.0, V45.1, V56.x |
| Liver disease | 070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 070.6, 070.9, 456.0–456.2, 570.x, 571.x, 572.2–572.8, 573.3, 573.4, 573.8, 573.9, V42.7 |
| Peptic ulcer disease excluding bleeding | 531.7, 531.9, 532.7, 532.9, 533.7, 533.9, 534.7, 534.9 |
| AIDS/HIV | 042.x–044.x |
| Lymphoma | 200.x–202.x, 203.0, 238.6 |
| Metastatic cancer | 196.x–199.x |
| Solid tumor without metastasis | 140.x–172.x, 174.x–195.x |
| Rheumatoid arthritis/collagen vascular diseases | 446.x, 701.0, 710.0–710.4, 710.8, 710.9, 711.2, 714.x, 719.3, 720.x, 725.x, 728.5, 728.89, 729.30 |
| Coagulopathy | 286.x, 287.1, 287.3–287.5 |
| Obesity ‡ | 278.0 |
| Weight loss | 260.x–263.x, 783.2, 799.4 |
| Fluid and electrolyte disorders | 253.6, 276.x |
| Blood loss anemia | 280.0 |
| Deficiency anemia | 280.1–280.9, 281.x |
| Alcohol abuse | 265.2, 291.1–291.3, 291.5–291.9, 303.0, 303.9, 305.0, 357.5, 425.5, 535.3, 571.0–571.3, 980.x, V11.3 |
| Drug abuse | 292.x, 304.x, 305.2–305.9, V65.42 |
| Psychoses | 293.8, 295.x, 296.04, 296.14, 296.44, 296.54, 297.x, 298.x |
| Depression | 296.2, 296.3, 296.5, 300.4, 309.x, 311 |
| \* The Elixhauser co-morbidity index includes 31 comorbidities.  † *Adapated from:* Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi JC, Saunders LD, Beck CA, Feasby TE, Ghali WA. Coding Algorithms for Defining Comorbidities in ICD-9-CM and ICD-10 Administrative Data. Med Care. 2005 Nov;43(11):1130-9.  ‡ 31 comorbidities are typically included in the Elixhauser comorbidity index. In our Elixhauser comorbidity index, we excluded the obesity comorbidity to prevent collinearity. This exclusion left a total of 30 comorbidities. | |

Fortin Y, Crispo JA, Cohen D, McNair DS, Mattison DR, Krewski D. External validation and comparison of two variants of the Elixhauser comorbidity measures for all-cause mortality. PLoS One. 2017 Mar 28;12(3):e0174379.

Epstein RH, Dexter F. Development and validation of a structured query language implementation of the Elixhauser comorbidity index. J Am Med Inform Assoc. 2017 Jul 1;24(4):845-850.

**eAppendix 7. SAS CODE used in Logistic Regression**

libname d "…\SepsisData\SASanalysis";

**data** sdata;

set d.Sepsis\_BMI\_Data;

**run**;

title 'GEE Unadjusted – Reference group = Normal Weight';

ods select GEEEmpPEst Estimates ;

**proc** **genmod** data=sdata descend ;

class hospital\_id bmi\_cat(ref="Normal")/ param=ref;

model death\_or\_hospice\_yn=bmi\_cat/ dist=bin;

estimate "Underweight vs Normal" bmi\_cat **0** **0** **0** **0** **1** / exp;

estimate "Overweight vs Normal" bmi\_cat **0** **0** **0** **1** **0** / exp;

estimate "Obese1 vs Normal" bmi\_cat **0** **1** **0** **0** **0** / exp;

estimate "Obese2 vs Normal" bmi\_cat **0** **0** **1** **0** **0** / exp;

estimate "Morbid Obese vs Normal" bmi\_cat **1** **0** **0** **0** **0** / exp;

repeated subject=hospital\_id / corr=cs ;

ods output Estimates=estim01a;

**run**;

title 'GEE Unadjusted – Reference group = Obese Category II Weight';

ods select GEEEmpPEst Estimates ;

**proc** **genmod** data=sdata descend ;

class hospital\_id bmi\_cat(ref="ObeseC2")/ param=ref;

model death\_or\_hospice\_yn=bmi\_cat/ dist=bin;

estimate "Underweight vs ObeseC2" bmi\_cat **0** **0** **0** **0** **1** / exp;

estimate "Normal vs ObeseC2" bmi\_cat **0** **1** **0** **0** **0** / exp;

estimate "Overweight vs ObeseC2" bmi\_cat **0** **0** **0** **1** **0** / exp;

estimate "Obese1 vs ObeseC2" bmi\_cat **0** **0** **1** **0** **0** / exp;

estimate "Morbid Obese vs ObeseC2" bmi\_cat **1** **0** **0** **0** **0** / exp;

repeated subject=hospital\_id / corr=cs ;

ods output Estimates=estim01b;

**run**;

title 'GEE Adjusted – Reference group = Normal Weight';

ods select GEEEmpPEst Estimates ;

**proc** **genmod** data=sdata descend ;

class hospital\_id bmi\_cat(ref="Normal") bed\_capacity(ref="500+") sepsis\_rate\_stratum(ref="low") urban\_rural\_status(ref="Rural") infection\_site\_full(ref="uti") gender(ref="M")

census\_region(ref="West") race(ref="WHITE") teaching\_facility\_ind(ref="0") icu(ref="N") bc\_positive\_yn(ref="N")

sofa\_sepsis\_bc\_infection\_type(ref="community") year(ref="2015") / param=ref;

model death\_or\_hospice\_yn=bmi\_cat bed\_capacity gender sepsis\_rate\_stratum urban\_rural\_status infection\_site\_full census\_region race teaching\_facility\_ind icu age bc\_positive\_yn sofa\_score sofa\_sepsis\_bc\_infection\_type year elixhauser\_score/ dist=bin;

estimate "Underweight vs Normal" bmi\_cat **0** **0** **0** **0** **1** / exp;

estimate "Overweight vs Normal" bmi\_cat **0** **0** **0** **1** **0** / exp;

estimate "Obese1 vs Normal" bmi\_cat **0** **1** **0** **0** **0** / exp;

estimate "Obese2 vs Normal" bmi\_cat **0** **0** **1** **0** **0** / exp;

estimate "Morbid Obese vs Normal" bmi\_cat **1** **0** **0** **0** **0** / exp;

repeated subject=hospital\_id / corr=cs ;

ods output Estimates=estim02a4;

**run**;

title 'GEE Adjusted – Reference group = Obese Category II Weight';

ods select GEEEmpPEst Estimates ;

**proc** **genmod** data=sdata descend ;

class hospital\_id bmi\_cat(ref="ObeseC2") bed\_capacity(ref="500+") sepsis\_rate\_stratum(ref="low") urban\_rural\_status(ref="Rural") infection\_site\_full(ref="uti") gender(ref="M") census\_region(ref="West") race(ref="WHITE") teaching\_facility\_ind(ref="0") icu(ref="N") bc\_positive\_yn(ref="N")

sofa\_sepsis\_bc\_infection\_type(ref="community") year(ref="2015") / param=ref;

model death\_or\_hospice\_yn=bmi\_cat bed\_capacity gender sepsis\_rate\_stratum urban\_rural\_status infection\_site\_full census\_region race teaching\_facility\_ind icu age bc\_positive\_yn sofa\_score sofa\_sepsis\_bc\_infection\_type year elixhauser\_score/ dist=bin;

estimate "Underweight vs ObeseC2" bmi\_cat **0** **0** **0** **0** **1** / exp;

estimate "Normal vs ObeseC2" bmi\_cat **0** **1** **0** **0** **0** / exp;

estimate "Overweight vs ObeseC2" bmi\_cat **0** **0** **0** **1** **0** / exp;

estimate "Obese1 vs ObeseC2" bmi\_cat **0** **0** **1** **0** **0** / exp;

estimate "Morbid Obese vs ObeseC2" bmi\_cat **1** **0** **0** **0** **0** / exp;

repeated subject=hospital\_id / corr=cs ;

ods output Estimates=estim02b4;

**run**;

**eAppendix 8. R Code used in Power Analysis**

library(powerMediation)

# SSizeLogisticBin(p1,p2,B,alpha,power)

# p1=P(mortality|Normal Weight)

# p2=P(mortality|Other Weight); Other Weight=(Underweight, Overweight, Obese Class I BMI, Obese Class II BMI, Obese Class II BMI)

# B=P(Other Weight)

# alpha: Type I error

# power= power

# Sample size calculation for Underweight vs. Normal Weight

# Proportion of Underweight in Sepsis Cohort = 6.4%

# Proportion of Normal weight in Sepsis Cohort = 33.0%

# Bivariate proportion of Underweight = 100 \* 6.4/(6.4+33.0) = 16.2 %

# Bivariate proportion of Normal weight = 100 \* 33 /(6.4+33.0) = 83.8 %

# Mortality of Underweight in Sepsis cohort = 30.7%

# Mortality of Normal weight in Sepsis cohort = 23.7%

# p1=P(mortality|Normal Weight)=0.237

# p2=P(mortality|Underweight)=0.307

# B=P(Underweight)=0.162

# alpha = 0.01

# power = 0.8

# Bivariate Required Sample Size

SSizeLogisticBin(0.237,0.307,0.162,alpha=0.01,power=0.8)

#3366

#Required Sample Size for the Full Sepsis Cohort

3366/(0.064 + 0.33)

#8544

**eAppendix 9: Assumptions of Logistic Regression**

[Logistic regression](http://www.statisticssolutions.com/academic-solutions/membership-resources/member-profile/data-analysis-plan-templates/data-analysis-plan-logistic-regression/)does not make many of the key assumptions of [linear regression](http://www.statisticssolutions.com/academic-solutions/membership-resources/member-profile/data-analysis-plan-templates/data-analysis-plan-linear-regression/)and [general linear models](http://www.statisticssolutions.com/academic-solutions/resources/directory-of-statistical-analyses/generalized-linear-models/)that are based on ordinary least squares algorithms – particularly regarding linearity, normality, homoscedasticity, and measurement level. We address each assumption below in detail.

1. Equal variances

Unlike in least squares estimation of normal-response models, variances are not assumed to be equal in the maximum likelihood estimation of generalized linear models. Therefore, we did not need to check homoscedasticity in the logistic regression.

1. Independence

As in ordinary regression, independence of the observations is assumed in the logistic regression. Autocorrelation or correlated clusters of observations may adversely affect the parameter variance estimates. However, in our data set, there are encounters coming from the same hospital. When the data are known to be correlated in clusters, the model can be fit using the Generalized Estimating Equations (GEE) method. In our analysis, we used the SAS PROG GENMOD with the REPEATED statement to fit the GEE model. The GEE method employs a White-like sandwich variance estimator, which accounts for the correlation.

1. Normal errors (residuals)

For generalized linear models in which the response distribution is not normal, the residuals from these models are also not normal. So, again there is no need to test for this condition when fitting the logistic regression model in SAS PROC GENMOD which is designed to fit such models.

## Predictor collinearity and ill-conditioned information matrix

In our multivariate logistic regression model, we included three continuous predictors (Age, SOFA score, and Elixhauser comorbidity index) and twelve categorical predictors (gender, ethnicity, admission year, census region, urban/ rural setting, bed capacity, teaching facility, volume of sepsis admissions, community vs. hospital-onset, infection site, bacteremia, ICU admission, and ICU type) as for control (adjustment) variables.

Unlike in normal-response models, the existence of collinearity does not necessarily imply ill-conditioning in generalized linear models. Extremely large standard errors for one or more of the estimated parameters and large off-diagonal values in the parameter covariance matrix or correlation matrix both suggest an ill-conditioned information matrix. However, these conditions can also happen for reasons not related to collinearity among the raw predictors.

One way to measure multicollinearity is the variance inflation factor (VIF), which assesses how much the variance of an estimated regression coefficient increases if your predictors are correlated. Unfortunately, the SAS PROC GENMOD does not provide VIF values when fitting a logistic regression model. However, we can still check for the multicollinearity by fitting a multiple linear regression model with all same 15 predictors. We generated a random response variable by simulation then fit the multiple linear regression model to produce VIF values. After examining the VIF values for all 15 predictor variables, we did not see any evidence of multicollinearity.

Additionally, we investigated how GEE method behaves if there is a high collinearity among the predictor variables. We simulated three variables such that each simulated variable is highly correlated (r=0.998) with one of the continuous predictors (Age, Sofa score, and Elixhauser score) in our model. We rerun the logistic regression including all 15 predictors and 3 simulated variables. We observe that there is not significant difference in the estimate of BMI categories (main factor) and the odd ratios. GEE method is very robust even there is high collinearity among the predictor variables.

1. Linearity

The logistic regression assumes linearity of independent variables and log odds.  Although this analysis does not require the dependent and independent variables to be related linearly, it requires that the independent variables are linearly related to the log odds. To test this assumption for the continuous predictors (Age, Sofa Score, and Elixhauser Score) in our model, we already performed a sensitivity analysis with the categorical version of these three variables in the full model. The results are reported in Online Data Supplement, p15. There is not much difference in the estimate of BMI categories (main factor) between the analysis 2.1 with the categorical predictors and the analysis 2.4 with the continuous predictors.

1. Large sample size

Logistic regression typically requires a large sample size. A general guideline is that you need at minimum of 10 cases with the least frequent outcome for each independent variable in your model. We have 15 independent variables in our model and the expected probability of least frequent outcome is .10. Therefore, 1500 (10\*15 / .10) cases are needed as a minimum sample size.

Our dataset has a total of 55 thousand encounters. With the 11,117 cases and 43,921 controls, we satisfy the large sample size assumption.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Table E1. Baseline characteristics of adult patients with sepsis across body mass index categories** | | | | | | | | | | | | | | | |
|  | **BMI categories** | | | | | | | | | | | | **All patients** | |
|  | **Underweight** | | **Normal** | | **Overweight** | | **Obese Class I** | | **Obese Class II** | | **Obese Class III** | |  | |
| **Body Mass Index** | **< 18.5 kg/m2** | | **18.5 - 24.9 kg/m2** | | **25.0 - 29.9 kg/m2** | | **30.0 - 34.9 kg/m2** | | **35.0 - 39.9 kg/m2** | | **> 40.0 kg/m2** | |  | |
|  | (n=3,520) | | (n=18,164) | | (n=15,193) | | (n=8,916) | | (n=4,364) | | (n=4,881) | | (n=55,038) | |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Age in years, median (IQR)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | 71 | (58-83) | 73 | (59-84) | 71 | (58-82) | 68 | (56-77) | 65 | (55-75) | 61 | (51-70) | 69 | (57-81) |
| **Gender, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *Male* | 1541 | (43.8) | 9410 | (51.8) | 8434 | (55.5) | 4560 | (51.1) | 1934 | (44.3) | 1769 | (36.2) | 27648 | (50.2) |
| **Ethnicity, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *Asian* | 93 | (2.6) | 415 | (2.3) | 193 | (1.3) | 71 | (0.8) | 18 | (0.4) | 17 | (0.3) | 807 | (1.5) |
| *Black* | 889 | (25.3) | 3317 | (18.3) | 2489 | (16.4) | 1543 | (17.3) | 833 | (19.1) | 991 | (20.3) | 10062 | (18.3) |
| *Hispanic* | 31 | (0.9) | 155 | (0.9) | 138 | (0.9) | 92 | (1.0) | 52 | (1.2) | 46 | (0.9) | 514 | (0.9) |
| *Other* | 94 | (2.7) | 608 | (3.3) | 612 | (4.0) | 342 | (3.8) | 159 | (3.6) | 169 | (3.5) | 1984 | (3.6) |
| *White* | 2413 | (68.6) | 13669 | (75.3) | 11761 | (77.4) | 6868 | (77) | 3302 | (75.7) | 3658 | (74.9) | 41671 | (75.7) |
| **Admission year, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *Pre-2010* | 257 | (7.3) | 1220 | (6.7) | 1004 | (6.6) | 572 | (6.4) | 264 | (6.0) | 344 | (7.0) | 3661 | (6.7) |
| *2011 - 2013* | 1977 | (56.2) | 9748 | (53.7) | 8004 | (52.7) | 4810 | (53.9) | 2378 | (54.5) | 2665 | (54.6) | 29582 | (53.7) |
| *2014 - 2015* | 1286 | (36.5) | 7196 | (39.6) | 6185 | (40.7) | 3534 | (39.6) | 1722 | (39.5) | 1872 | (38.4) | 21795 | (39.6) |
| **Admission Source, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *Acute care hospital* | 107 | (3.0) | 792 | (4.4) | 768 | (5.0) | 516 | (5.8) | 282 | (6.5) | 309 | (6.4) | 2774 | (5.0) |
| *Subacute care facility* | 261 | (7.5) | 1352 | (7.4) | 1058 | (7.0) | 527 | (88.3) | 266 | (6.1) | 265 | (5.4) | 3729 | (6.8) |
| *Unspecified/ non-facility origin* | 3152 | (89.5) | 16020 | (88.2) | 13367 | (88.0) | 7873 | (5.9) | 3816 | (87.4) | 4307 | (88.2) | 48535 | (88.2) |
| **Census Region, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *Midwest* | 661 | (18.8) | 2914 | (16.0) | 2354 | (15.5) | 1530 | (17.2) | 820 | (18.8) | 1002 | (20.5) | 9281 | (16.9) |
| *Northeast* | 1015 | (28.8) | 6238 | (34.3) | 5560 | (36.6) | 3092 | (34.7) | 1434 | (32.9) | 1520 | (31.1) | 18859 | (34.3) |
| *South* | 1563 | (44.4) | 7362 | (40.5) | 5894 | (38.8) | 3485 | (39.1) | 1712 | (39.2) | 1924 | (39.4) | 21940 | (39.9) |
| *West* | 281 | (8.0) | 1650 | (9.1) | 1385 | (9.1) | 809 | (9.1) | 398 | (9.1) | 435 | (8.9) | 4958 | (9.0) |
| **Urban-rural setting, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *Urban setting* | 2565 | (72.9) | 12702 | (69.9) | 10606 | (69.8) | 6433 | (72.2) | 3285 | (75.3) | 3803 | (77.9) | 39394 | (71.6) |
| *Rural setting* | 955 | (27.1) | 5462 | (30.1) | 4587 | (30.2) | 2483 | (27.8) | 1079 | (24.7) | 1078 | (22.1) | 15644 | (28.4) |
| **Facility bed capacity, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *< 100* | 180 | (5.1) | 1003 | (5.5) | 822 | (5.4) | 528 | (5.9) | 253 | (5.8) | 281 | (5.8) | 3067 | (5.6) |
| *100-199* | 453 | (12.9) | 2224 | (12.2) | 1841 | (12.1) | 1049 | (11.8) | 447 | (10.2) | 581 | (11.9) | 6595 | (12.0) |
| *200-299* | 866 | (24.6) | 3999 | (22.0) | 3226 | (21.2) | 1909 | (21.4) | 955 | (21.9) | 1089 | (22.3) | 12044 | (21.9) |
| *300-499* | 1226 | (34.8) | 5849 | (32.2) | 4829 | (31.8) | 2885 | (32.4) | 1509 | (34.6) | 1715 | (35.1) | 18013 | (32.7) |
| *500+* | 795 | (22.6) | 5089 | (28.0) | 4475 | (29.5) | 2545 | (28.5) | 1200 | (27.5) | 1215 | (24.9) | 15319 | (27.8) |
| **Type of facility, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *Teaching* | 2816 | (80.0) | 14430 | (79.4) | 12214 | (80.4) | 7137 | (80.0) | 3541 | (81.1) | 3925 | (80.4) | 44063 | (80.1) |
| *Non-teaching* | 704 | (20.0) | 3734 | (20.6) | 2979 | (19.6) | 1779 | (20.0) | 823 | (18.9) | 956 | (19.6) | 10975 | (19.9) |
| **Volume of sepsis admissions at facility, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *Low* | 166 | (4.7) | 802 | (4.4) | 675 | (4.4) | 484 | (5.4) | 253 | (5.8) | 253 | (5.2) | 2633 | (4.8) |
| *Medium* | 956 | (27.2) | 5171 | (28.5) | 4337 | (28.5) | 2564 | (28.8) | 1287 | (29.5) | 1421 | (29.1) | 15736 | (28.6) |
| *High* | 2398 | (68.1) | 12191 | (67.1) | 10181 | (67.0) | 5868 | (65.8) | 2824 | (64.7) | 3207 | (65.7) | 36669 | (66.6) |
| **Infection onset, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *Community onset* | 3096 | (88.0) | 15365 | (84.6) | 12653 | (83.3) | 7334 | (82.3) | 3675 | (84.2) | 4184 | (85.7) | 46307 | (84.1) |
| *Hospital onset \** | 424 | (12.0) | 2799 | (15.4) | 2540 | (16.7) | 1582 | (17.7) | 689 | (15.8) | 697 | (14.3) | 8731 | (15.9) |
| **Site of Infection, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *intra-abdominal* | 185 | (5.3) | 1407 | (7.7) | 1242 | (8.2) | 742 | (8.3) | 353 | (8.1) | 291 | (6.0) | 4220 | (7.7) |
| *multiple sites* | 550 | (15.6) | 2728 | (15.0) | 2216 | (14.6) | 1247 | (14.0) | 672 | (15.4) | 795 | (16.3) | 8208 | (14.9) |
| *pneumonia* | 1039 | (29.5) | 4671 | (25.7) | 3677 | (24.2) | 2155 | (24.2) | 996 | (22.8) | 1022 | (20.9) | 13560 | (24.6) |
| *septicaemia/bacteremia* | 322 | (9.1) | 1395 | (7.7) | 1227 | (8.1) | 657 | (7.4) | 340 | (7.8) | 308 | (6.3) | 4249 | (7.7) |
| *skin/ soft tissue* | 81 | (2.3) | 681 | (3.7) | 743 | (4.9) | 527 | (5.9) | 353 | (8.1) | 616 | (12.6) | 3001 | (5.5) |
| *urinary tract infection* | 601 | (17.1) | 3026 | (16.7) | 2452 | (16.1) | 1356 | (15.2) | 639 | (14.6) | 775 | (15.9) | 8849 | (16.1) |
| *unspecified site of infection* | 742 | (21.1) | 4256 | (23.4) | 3636 | (23.9) | 2232 | (25.0) | 1011 | (23.2) | 1074 | (22.0) | 12951 | (23.5) |
| **Blood culture, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *Positive* | 609 | (17.3) | 3039 | (16.7) | 2558 | (16.8) | 1537 | (17.2) | 750 | (17.2) | 913 | (18.7) | 9406 | (17.1) |
| *Negative* | 2911 | (82.7) | 15125 | (83.3) | 12635 | (83.2) | 7379 | (82.8) | 3614 | (82.8) | 3968 | (81.3) | 45632 | (82.9) |
| **SOFA score at admission, median (IQR)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *SOFA Renal* | 0 | (0-1) | 0 | (0-1) | 1 | (0-1) | 1 | (0-2) | 1 | (0-2) | 1 | (0-2) | 1 | (0-1) |
| *SOFA hepatic* | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) |
| *SOFA Coag* | 0 | (0-0) | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) | 0 | (0-0) | 0 | (0-0) | 0 | (0-1) |
| *SOFA cardiovascular* | 1 | (0-1) | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) |
| *SOFA GCS* | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) |
| *SOFA pulm* | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) | 0 | (0-2) | 0 | (0-1) |
| *SOFA Total* | 3 | (2-5) | 3 | (2-5) | 3 | (2-5) | 3 | (2-5) | 3 | (2-5) | 3 | (2-5) | 3 | (2-5) |
| **Elixhauser score, median (IQR) \*\*** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | 4 | (3-5) | 4 | (3-6) | 4 | (3-6) | 4 | (3-6) | 4 | (3-6) | 4 | (3-6) | 4 | (3-6) |
| **Albumin, median (IQR)** | 3 | (2.5-3.5) | 3.2 | (2.6-3.6) | 3.2 | (2.7-3.7) | 3.3 | (2.8-3.7) | 3.2 | (2.7-3.7) | 3.2 | (2.8-3.6) | 3.2 | (2.7-3.7) |
| *Data available (%)* | 2690 | (76.4) | 13593 | (74.8) | 11408 | (75.1) | 6691 | (75.0) | 3259 | (74.7) | 3671 | (75.2) | 41312 | (75.1) |
| **Admitted to ICU, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *Yes* | 907 | (25.8) | 4554 | (25.1) | 4006 | (26.4) | 2419 | (27.1) | 1200 | (27.5) | 1425 | (29.2) | 14511 | (26.4) |
| **ICU type, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *Coronary/ Cardiac ICU* | 86 | (2.4) | 481 | (2.6) | 464 | (3.1) | 321 | (3.6) | 187 | (4.3) | 176 | (3.6) | 1715 | (3.1) |
| *Medical ICU* | 108 | (3.1) | 530 | (2.9) | 483 | (3.2) | 261 | (2.9) | 129 | (3.0) | 164 | (3.4) | 1675 | (3.0) |
| *Other/ Unspecified/ Neurology ICU* | 654 | (18.6) | 3174 | (17.5) | 2657 | (17.5) | 1593 | (17.9) | 770 | (17.6) | 943 | (19.3) | 9791 | (17.8) |
| *Surgical ICU* | 59 | (1.7) | 369 | (2.0) | 402 | (2.6) | 244 | (2.7) | 114 | (2.6) | 142 | (2.9) | 1330 | (2.4) |
| *Not ICU* | 2613 | (74.2) | 13610 | (74.9) | 11187 | (73.6) | 6497 | (72.9) | 3164 | (72.5) | 3456 | (70.8) | 40527 | (73.6) |
| **Explicit sepsis diagnosis (ICD-9 code), n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *Sepsis* | 1386 | (39.4) | 6692 | (36.8) | 5456 | (35.9) | 3066 | (34.4) | 1556 | (35.7) | 1795 | (36.8) | 19951 | (36.3) |
| *Severe sepsis* | 765 | (21.7) | 3412 | (18.8) | 2903 | (19.1) | 1625 | (18.2) | 835 | (19.1) | 976 | (20.0) | 10516 | (19.1) |
| *Septic shock* | 493 | (14.0) | 2262 | (12.5) | 1847 | (12.2) | 1083 | (12.1) | 551 | (12.6) | 639 | (13.1) | 6875 | (12.5) |
| **Timing of antibiotic initiation, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *2 days before blood culture* | 115 | (3.3) | 840 | (4.6) | 760 | (5.0) | 425 | (4.8) | 216 | (4.9) | 224 | (4.6) | 2580 | (4.7) |
| *1 day before blood cultures* | 237 | (6.7) | 1470 | (8.1) | 1261 | (8.3) | 821 | (9.2) | 369 | (8.5) | 394 | (8.1) | 4552 | (8.3) |
| *Same day as blood cultures* | 2720 | (77.3) | 13314 | (73.3) | 11028 | (72.6) | 6346 | (71.2) | 3153 | (72.3) | 3606 | (73.9) | 40167 | (73) |
| *1 day after blood cultures* | 326 | (9.3) | 1810 | (10.0) | 1522 | (10.0) | 908 | (10.2) | 437 | (10.0) | 462 | (9.5) | 5465 | (9.9) |
| *2 days after blood cultures* | 122 | (3.5) | 730 | (4.0) | 622 | (4.1) | 416 | (4.7) | 189 | (4.3) | 195 | (4.0) | 2274 | (4.1) |
| **Procedures at or after sepsis diagnosis, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *Arterial line insertion* | 131 | (3.7) | 712 | (3.9) | 644 | (4.2) | 403 | (4.5) | 244 | (5.6) | 269 | (5.5) | 2403 | (4.4) |
| *Bronchoscopy* | 227 | (6.4) | 887 | (4.9) | 722 | (4.8) | 464 | (5.2) | 214 | (4.9) | 208 | (4.3) | 2722 | (4.9) |
| *Central venous catheter insertion* | 770 | (21.9) | 3930 | (21.6) | 3524 | (23.2) | 2142 | (24.0) | 1179 | (27.0) | 1415 | (29.0) | 12960 | (23.5) |
| *Chest tube insertion* | 150 | (4.3) | 835 | (4.6) | 696 | (4.6) | 363 | (4.1) | 177 | (4.1) | 118 | (2.4) | 2339 | (4.2) |
| *Computerized tomography* | 71 | (2.0) | 574 | (3.2) | 471 | (3.1) | 264 | (3.0) | 111 | (2.5) | 113 | (2.3) | 1604 | (2.9) |
| *Dialysis procedure* | 209 | (5.9) | 1252 | (6.9) | 1108 | (7.3) | 733 | (8.2) | 425 | (9.7) | 452 | (9.3) | 4179 | (7.6) |
| *Endotracheal intubation* | 523 | (14.9) | 2492 | (13.7) | 2125 | (14.0) | 1265 | (14.2) | 658 | (15.1) | 735 | (15.1) | 7798 | (14.2) |
| *Lumbar puncture* | 43 | (1.2) | 302 | (1.7) | 240 | (1.6) | 152 | (1.7) | 74 | (1.7) | 72 | (1.5) | 883 | (1.6) |
| *Magnetic resonance imaging* | 26 | (0.7) | 160 | (0.9) | 168 | (1.1) | 106 | (1.2) | 52 | (1.2) | 37 | (0.8) | 549 | (1.0) |
| *Paracentesis* | 68 | (1.9) | 434 | (2.4) | 409 | (2.7) | 233 | (2.6) | 115 | (2.6) | 83 | (1.7) | 1342 | (2.4) |
| *Pulmonary artery catheter insertion* | 5 | (0.1) | 43 | (0.2) | 82 | (0.5) | 37 | (0.4) | 21 | (0.5) | 25 | (0.5) | 213 | (0.4) |
| *Tracheostomy* | 56 | (1.6) | 268 | (1.5) | 248 | (1.6) | 169 | (1.9) | 74 | (1.7) | 107 | (2.2) | 922 | (1.7) |
| Hospital-onset sepsis was defined as sepsis onset occurring 3 days or more after the day of admission; or as sepsis onset within 3 days of admission if transferred from another institution (nursing home, long-term care or another acute-care hospital). | | | | | | | | | | | | | | |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Table E2. Proportions of patients with co-morbid illnesses as defined by the Elixhauser Co-morbidity Index in each body mass index category** | | | | | | | | | | | | | |
|  | **Elixhauser Co-morbidity** | **Body mass index category** | | | | | | | | | | | |
|  |  | **Underweight** (n=3,520) | | **Normal weight** (n=18,164) | | **Overweight** (n=15,193) | | **Obese** **Class I** (n=8,916) | | **Obese Class II** (n=4,364) | | **Obese Class III** (n=4,881) | |
|  |  | n | % | n | % | n | % | n | % | n | % | n | % |
| 1 | Congestive Heart Failure | 691 | 19.6 | 4,729 | 26.0 | 4,345 | 28.6 | 2,734 | 30.7 | 1,433 | 32.8 | 1,797 | 36.8 |
| 2 | Cardiac Arrhythmia | 928 | 26.4 | 5,735 | 31.6 | 4,797 | 31.6 | 2,758 | 30.9 | 1,281 | 29.4 | 1,361 | 27.9 |
| 3 | Valvular Disease | 293 | 8.3 | 2,040 | 11.2 | 1,759 | 11.6 | 935 | 10.5 | 412 | 9.4 | 348 | 7.1 |
| 4 | Pulmonary Circulation Disorders | 256 | 7.3 | 1,498 | 8.2 | 1,331 | 8.8 | 824 | 9.2 | 444 | 10.2 | 642 | 13.2 |
| 5 | Peripheral Vascular Disorders | 380 | 10.8 | 1,980 | 10.9 | 1,676 | 11.0 | 993 | 11.1 | 438 | 10.0 | 372 | 7.6 |
| 6 | Hypertension Uncomplicated | 1,317 | 37.4 | 7,321 | 40.3 | 6,663 | 43.9 | 4,154 | 46.6 | 2,039 | 46.7 | 2,266 | 46.4 |
| 7 | Hypertension Complicated | 572 | 16.3 | 3,588 | 19.8 | 3,421 | 22.5 | 2,108 | 23.6 | 1,098 | 25.2 | 1,235 | 25.3 |
| 8 | Paralysis | 162 | 4.6 | 740 | 4.1 | 600 | 3.9 | 333 | 3.7 | 141 | 3.2 | 124 | 2.5 |
| 9 | Other Neurological Disorders | 450 | 12.8 | 2,230 | 12.3 | 1,673 | 11.0 | 853 | 9.6 | 379 | 8.7 | 322 | 6.6 |
| 10 | Chronic Pulmonary Disease | 1,463 | 41.6 | 6,242 | 34.4 | 5,098 | 33.6 | 3,227 | 36.2 | 1,750 | 40.1 | 2,235 | 45.8 |
| 11 | Diabetes Uncomplicated | 477 | 13.6 | 3,542 | 19.5 | 3,997 | 26.3 | 2,959 | 33.2 | 1,714 | 39.3 | 2,101 | 43.0 |
| 12 | Diabetes Complicated | 130 | 3.7 | 1,010 | 5.6 | 1,237 | 8.1 | 947 | 10.6 | 590 | 13.5 | 736 | 15.1 |
| 13 | Hypothyroidism | 419 | 11.9 | 2,455 | 13.5 | 2,099 | 13.8 | 1,273 | 14.3 | 690 | 15.8 | 795 | 16.3 |
| 14 | Renal Failure | 710 | 20.2 | 4,198 | 23.1 | 3,917 | 25.8 | 2,392 | 26.8 | 1,226 | 28.1 | 1,377 | 28.2 |
| 15 | Liver Disease | 144 | 4.1 | 1,041 | 5.7 | 961 | 6.3 | 595 | 6.7 | 297 | 6.8 | 290 | 5.9 |
| 16 | Peptic Ulcer Disease excluding bleeding | 61 | 1.7 | 270 | 1.5 | 219 | 1.4 | 118 | 1.3 | 53 | 1.2 | 44 | 0.9 |
| 17 | AIDS/HIV | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| 18 | Lymphoma | 69 | 2.0 | 503 | 2.8 | 422 | 2.8 | 200 | 2.2 | 95 | 2.2 | 68 | 1.4 |
| 19 | Metastatic Cancer | 301 | 8.6 | 1,248 | 6.9 | 878 | 5.8 | 433 | 4.9 | 169 | 3.9 | 123 | 2.5 |
| 20 | Solid Tumor without Metastasis | 428 | 12.2 | 1,621 | 8.9 | 1,200 | 7.9 | 565 | 6.3 | 211 | 4.8 | 170 | 3.5 |
| 21 | Rheumatoid Arthritis/collagen | 130 | 3.7 | 608 | 3.3 | 573 | 3.8 | 327 | 3.7 | 169 | 3.9 | 171 | 3.5 |
| 22 | Coagulopathy | 379 | 10.8 | 2,381 | 13.1 | 1,945 | 12.8 | 1,081 | 12.1 | 474 | 10.9 | 458 | 9.4 |
| 23 | Weight Loss | 1,198 | 34.0 | 3,015 | 16.6 | 1,684 | 11.1 | 796 | 8.9 | 402 | 9.2 | 371 | 7.6 |
| 24 | Fluid and Electrolyte Disorders | 2,263 | 64.3 | 10,715 | 59.0 | 8,606 | 56.6 | 4,789 | 53.7 | 2,348 | 53.8 | 2,542 | 52.1 |
| 25 | Blood Loss Anemia | 54 | 1.5 | 266 | 1.5 | 229 | 1.5 | 118 | 1.3 | 73 | 1.7 | 55 | 1.1 |
| 26 | Deficiency Anemia | 218 | 6.2 | 956 | 5.3 | 722 | 4.8 | 402 | 4.5 | 237 | 5.4 | 233 | 4.8 |
| 27 | Alcohol Abuse | 277 | 7.9 | 1,396 | 7.7 | 1,057 | 7.0 | 556 | 6.2 | 202 | 4.6 | 141 | 2.9 |
| 28 | Drug Abuse | 158 | 4.5 | 890 | 4.9 | 694 | 4.6 | 378 | 4.2 | 177 | 4.1 | 145 | 3.0 |
| 29 | Psychoses | 145 | 4.1 | 721 | 4.0 | 593 | 3.9 | 345 | 3.9 | 163 | 3.7 | 194 | 4.0 |
| 30 | Depression | 512 | 14.5 | 2,483 | 13.7 | 2,110 | 13.9 | 1,346 | 15.1 | 739 | 16.9 | 829 | 17.0 |

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| **eTable 3. Clinical outcomes among adult patients with sepsis across BMI categories** | | | | | | | | | | | | |
|  | **BMI categories** | | | | | | | | | | | |
|  | **Underweight** | | **Normal** | | **Overweight** | | **Obese Class I** | | **Obese Class II** | | **Obese Class III** | | **All patients** | |
| **Body Mass Index** | **< 18.5 kg/m2** | | **18.5 - 24.9 kg/m2** | | **25.0 - 29.9 kg/m2** | | **30.0 - 34.9 kg/m2** | | **35.0 - 39.9 kg/m2** | | **> 40.0 kg/m2** | |  | |
|  | (n=3,520) | | (n=18,164) | | (n=15,193) | | (n=8,916) | | (n=4,364) | | (n=4,881) | | (n=55,038) | |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **In-hospital death, n (%)** | 711 | (20.2) | 2998 | (16.5) | 2150 | (14.2) | 1107 | (12.4) | 509 | (11.7) | 592 | (12.1) | 8067 | (14.7) |
| **Discharge to hospice, n (%)** | 369 | (10.5) | 1302 | (7.2) | 747 | (4.9) | 351 | (3.9) | 169 | (3.9) | 112 | (2.3) | 3050 | (5.5) |
| **Short-term mortality (death or hospice), n (%)** | 1080 | (30.7) | 4300 | (23.7) | 2897 | (19.1) | 1458 | (16.4) | 678 | (15.5) | 704 | (14.4) | 11117 | (20.2) |
| **Adjusted odds ratio of mortality**  **(death or hospice), (95% CI)** | 1.62\* | (1.5-1.74) | **Reference** | | 0.73\* | (0.7-0.77) | 0.61\* | (0.57-0.66) | 0.61\* | (0.55-0.67) | 0.65\* | (0.59-0.71) | - |  |
| **Adjusted odds ratio of mortality**  **(death or hospice), (95% CI)** | 2.67\* | (2.37-3) | 1.65\* | (1.5-1.81) | 1.21\* | (1.1-1.32) | 1.01 | (0.92-1.12) | **Reference** | | 1.07 | (0.98-1.17) | - |  |
| **Age at death, median (IQR)** | 76 | (62-86) | 77 | (64-86) | 75 | (63-84) | 70 | (60-79) | 69 | (57-76) | 64 | (54-72) | 73 | (62-84) |
| **ICU length of stay if admitted to ICU, median (IQR)** | 9 | (5-16) | 9 | (6-15) | 10 | (6-16) | 9 | (6-16) | 10 | (6-17) | 9 | (6-15) | 9 | (6-15) |
| **Hospital length of stay, median (IQR)** | 8 | (5-13) | 8 | (5-13) | 8 | (6-14) | 8 | (6-14) | 8 | (6-14) | 8 | (6-13) | 8 | (6-13) |
| Key:  Reference = BMI category that other BMI categories are compared to  \* P-value < 0.05 | | | | | | | | | | | | | | |

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| **Table E4 Comparison of baseline characteristics for patients with and without body mass index data** | | | | |
| **Variables** | **Adults with BMI data** | | **Adults without BMI data** | |
|  | (n=55,038) | | (n=83,473) | |
| **Age in years, median (IQR)** | 69 | (57-81) | 68 | (56-79) |
| **Gender, n (%)** |  |  |  |  |
| *Male* | 27648 | (50.2) | 41908 | (50.2) |
| **Ethnicity, n (%)** |  |  |  |  |
| *Asian* | 807 | (1.5) | 821 | (1) |
| *Black* | 10062 | (18.3) | 15729 | (18.8) |
| *Hispanic* | 514 | (0.9) | 1483 | (1.8) |
| *Other* | 1984 | (3.6) | 2553 | (3.1) |
| *Unknown* | 0 | (0) | 2504 | (3) |
| *White* | 41671 | (75.7) | 60383 | (72.3) |
| **Admission year, n (%)** |  |  |  |  |
| *Pre-2010* | 3661 | (6.7) | 36104 | (43.3) |
| *2011 - 2013* | 29582 | (53.7) | 33722 | (40.4) |
| *2014 - 2015* | 21795 | (39.6) | 13647 | (16.3) |
| **Census Region, n (%)** |  |  |  |  |
| *Midwest* | 9281 | (16.9) | 10782 | (12.9) |
| *Northeast* | 18859 | (34.3) | 32669 | (39.1) |
| *South* | 21940 | (39.9) | 32485 | (38.9) |
| *West* | 4958 | (9) | 7537 | (9) |
| **Urban-rural setting, n (%)** |  |  |  |  |
| *Urban setting* | 39394 | (71.6) | 69524 | (83.3) |
| *Rural setting* | 15644 | (28.4) | 13949 | (16.7) |
| **Facility bed capacity, n (%)** |  |  |  |  |
| *< 100* | 3067 | (5.6) | 5434 | (6.5) |
| *100-199* | 6595 | (12) | 11458 | (13.7) |
| *200-299* | 12044 | (21.9) | 21794 | (26.1) |
| *300-499* | 18013 | (32.7) | 20524 | (24.6) |
| *500+* | 15319 | (27.8) | 24263 | (29.1) |
| **Type of facility, n (%)** |  |  |  |  |
| *Teaching* | 44063 | (80.1) | 62342 | (74.8) |
| *Non-teaching* | 10975 | (19.9) | 20965 | (25.2) |
| **Volume of sepsis admissions at facility, n (%)** |  |  |  |  |
| *Low* | 2633 | (4.8) | 14275 | (17.1) |
| *Medium* | 15736 | (28.6) | 23015 | (27.6) |
| *High* | 36669 | (66.6) | 46183 | (55.3) |
| **Infection onset, n (%)** |  |  |  |  |
| *Community onset* | 46307 | (84.1) | 72026 | (86.3) |
| *Hospital onset* | 8731 | (15.9) | 11447 | (13.7) |
| **Site of Infection, n (%)** |  |  |  |  |
| *intra-abdominal* | 4220 | (7.7) | 6146 | (7.4) |
| *multiple sites* | 8208 | (14.9) | 9553 | (11.4) |
| *pneumonia* | 13560 | (24.6) | 15019 | (18) |
| *septicaemia/bacteremia* | 4249 | (7.7) | 7387 | (8.8) |
| *skin/ soft tissue* | 3001 | (5.5) | 3923 | (4.7) |
| *urinary tract infection* | 8849 | (16.1) | 12495 | (15) |
| *unspecified site of infection* | 12951 | (23.5) | 28950 | (34.7) |
| **Blood culture, n (%)** |  |  |  |  |
| *Positive* | 9406 | (17.1) | 17642 | (21.1) |
| *Negative* | 45632 | (82.9) | 65831 | (78.9) |
| **SOFA score at admission, median (IQR)** |  |  |  |  |
| *SOFA Renal* | 1 | (0-1) | 1 | (0-2) |
| *SOFA hepatic* | 0 | (0-0) | 0 | (0-1) |
| *SOFA Coag* | 0 | (0-1) | 0 | (0-1) |
| *SOFA cardiovascular* | 0 | (0-1) | 0 | (0-1) |
| *SOFA GCS* | 0 | (0-1) | 0 | (0-0) |
| *SOFA pulm* | 0 | (0-1) | 0 | (0-1) |
| *SOFA Total* | 3 | (2-5) | 3 | (2-5) |
| **Elixhauser score, median (IQR)** | 4 | (3-6) | 4 | (2-5) |
| **Albumin, median (IQR)** |  |  |  |  |
|  | 3.2 | (2.7-3.7) | 3.1 | (2.6-3.6) |
| *Data available (%)* | 41312 | (75.1) | 61738 | (74.0) |
| **Admitted to ICU, n (%)** | 14511 | (26.4) | 23229 | (27.8) |
| **ICU type, n (%)** |  |  |  |  |
| *Coronary/ Cardiac ICU* | 1715 | (3.1) | 3369 | (4) |
| *Medical ICU* | 1675 | (3) | 2328 | (2.8) |
| *Other/ Unspecified/ Neurology ICU* | 9791 | (17.8) | 15669 | (18.8) |
| *Surgical ICU* | 1330 | (2.4) | 1863 | (2.2) |
| *Not ICU* | 40527 | (73.6) | 60244 | (72.2) |
| **Septic shock, n (%)** | 6875 | (12.5) | 9957 | (11.9) |
| **Hospital Length of Stay, median (IQR)** | 8 | (6-13) | 9 | (6-15) |
| **ICU Length of Stay if in ICU, median (IQR)** | 9 | (6-15) | 10 | (6-17) |
| **In-hospital death, n (%)** | 8067 | (14.7) | 12999 | (15.6) |
| **Discharge to hospice, n (%)** | 3050 | (5.5) | 4065 | (4.9) |
| **Mortality (death or hospice), n (%)** | 11117 | (20.2) | 17064 | (20.4) |
| **Antibiotic administration, n (%)** |  |  |  |  |
| *-2* | 2580 | (4.7) | 4091 | (4.9) |
| *-1* | 4552 | (8.3) | 7283 | (8.7) |
| *0* | 40167 | (73) | 61535 | (73.7) |
| *1* | 5465 | (9.9) | 8017 | (9.6) |
| *2* | 2274 | (4.1) | 2547 | (3.1) |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
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| **Table E5: Sensitivity Analyses** | | | | | | | | | | | | | | | | | | | |
|  | **Variables** | **Total** | | | | | |  | **BMI categories** | | | | | | | | | | |
|  |  |  | | | | | | **Underweight** | | **Normal** | | **Overweight** | | **Obese Class I** | | **Obese Class II** | | **Obese Class III** | |
|  | **Body Mass Index** |  | | | | | | **< 18.5 kg/m2** | | **18.5 - 24.9 kg/m2** | | **25.0 - 29.9 kg/m2** | | **30.0 - 34.9 kg/m2** | | **35.0 - 39.9 kg/m2** | | **> 40.0 kg/m2** | |
|  |  | (n=55,038) | | | | | | (n=3,520) | | (n=18,164) | | (n=15,193) | | (n=8,916) | | (n=4,364) | | (n=4,881) | |
|  | **In-Hospital mortality (death or hospice), n (%)** |  | | | | | | | | | | | | | | | | | |
|  | *Yes* | 11,117 | | (20.2) | | | | 1,080 | (30.7) | 4,300 | (23.7) | 2,897 | (19.1) | 1,458 | (16.4) | 678 | (15.5) | 704 | (14.4) |
| **Analysis** | |  | |  | | | |  |  |  |  |  |  |  |  |  |  |  |  |
| **1** | *Unadjusted odds ratio, (95% CI)* |  | |  | | | | 1.45\* | (1.34-1.57) | **Ref** |  | 0.77\* | (0.73-0.81) | 0.63\* | (0.58-0.68) | 0.59\* | (0.54-0.65) | 0.55\* | (0.49-0.62) |
|  | *Unadjusted odds ratio, (95% CI)* |  | |  | | | | 2.45\* | (2.14-2.8) | 1.69\* | (1.54-1.86) | 1.3\* | (1.19-1.42) | 1.06 | (0.97-1.17) | **Ref** |  | 0.94 | (0.85-1.02) |
| **2.1** | *Adjusted odds ratio, (95% CI)* | With Catg Age & Sofa Score & Elix | | | | | | 1.57\* | (1.46-1.69) | **Ref** |  | 0.75\* | (0.71-0.79) | 0.63\* | (0.59-0.68) | 0.62\* | (0.57-0.68) | 0.67\* | (0.61-0.73) |
|  | *Adjusted odds ratio, (95% CI)* | With Catg Age & Sofa Score & Elix | | | | | | 2.52\* | (2.24-2.83) | 1.6\* | (1.47-1.75) | 1.2\* | (1.1-1.3) | 1.01 | (0.92-1.1) | **Ref** |  | 1.07 | (0.98-1.16) |
| **2.2** | *Adjusted odds ratio, (95% CI)* | With Cont. Age & Sofa Score & Catg Elix | | | | | | 1.62\* | (1.5-1.74) | **Ref** |  | 0.73\* | (0.7-0.77) | 0.62\* | (0.57-0.66) | 0.61\* | (0.56-0.67) | 0.65\* | (0.6-0.71) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Age and Sofa Score & Catg Elix | | | | | | 2.66\* | (2.36-2.99) | 1.64\* | (1.5-1.8) | 1.2\* | (1.1-1.31) | 1.01 | (0.92-1.12) | **Ref** |  | 1.07 | (0.98-1.17) |
| **2.3** | *Adjusted odds ratio, (95% CI)* | With Catg Age & Sofa Score & Cont Elix | | | | | | 1.57\* | (1.46-1.69) | **Ref** |  | 0.75\* | (0.71-0.79) | 0.63\* | (0.59-0.68) | 0.62\* | (0.57-0.68) | 0.66\* | (0.61-0.72) |
|  | *Adjusted odds ratio, (95% CI)* | With Catg Age & Sofa Score & Cont Elix | | | | | | 2.52\* | (2.24-2.84) | 1.6\* | (1.47-1.75) | 1.2\* | (1.1-1.3) | 1.01 | (0.92-1.1) | **Ref** |  | 1.06 | (0.98-1.15) |
| **2.4** | *Adjusted odds ratio, (95% CI)* | With Cont. Age & Sofa Score & Cont Elix | | | | | | 1.62\* | (1.5-1.74) | **Ref** |  | 0.73\* | (0.7-0.77) | 0.61\* | (0.57-0.66) | 0.61\* | (0.55-0.67) | 0.65\* | (0.59-0.71) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Age and Sofa Score & Cont Elix | | | | | | 2.67\* | (2.37-3) | 1.65\* | (1.5-1.81) | 1.21\* | (1.1-1.32) | 1.01 | (0.92-1.12) | **Ref** |  | 1.07 | (0.98-1.17) |
|  | ***bc\_positive=Yes (N=9,406)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **3** | *Unadjusted odds ratio, (95% CI)* |  | |  | | | | 1.48\* | (1.25-1.75) | **Ref** |  | 0.71\* | (0.63-0.81) | 0.71\* | (0.61-0.83) | 0.64\* | (0.52-0.78) | 0.6\* | (0.5-0.73) |
|  | *Unadjusted odds ratio, (95% CI)* |  | |  | | | | 2.33\* | (1.79-3.02) | 1.57\* | (1.28-1.93) | 1.12 | (0.9-1.4) | 1.12 | (0.91-1.38) | **Ref** |  | 0.95 | (0.74-1.22) |
| **3.1** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.71\* | (1.42-2.05) | **Ref** |  | 0.71\* | (0.62-0.81) | 0.71\* | (0.61-0.84) | 0.67\* | (0.55-0.82) | 0.7\* | (0.59-0.84) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.53\* | (1.93-3.32) | 1.48\* | (1.21-1.81) | 1.05 | (0.84-1.32) | 1.05 | (0.86-1.3) | **Ref** |  | 1.04 | (0.82-1.31) |
|  | ***bc\_positive=No (N=45,632)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **4** | *Unadjusted odds ratio, (95% CI)* |  | |  | | | | 1.44\* | (1.31-1.59) | **Ref** |  | 0.78\* | (0.73-0.82) | 0.6\* | (0.55-0.66) | 0.57\* | (0.52-0.64) | 0.53\* | (0.47-0.6) |
|  | *Unadjusted odds ratio, (95% CI)* |  | |  | | | | 2.51\* | (2.13-2.96) | 1.74\* | (1.56-1.94) | 1.35\* | (1.21-1.5) | 1.05 | (0.94-1.17) | **Ref** |  | 0.92 | (0.82-1.03) |
| **4.1** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.55\* | (1.42-1.7) | **Ref** |  | 0.75\* | (0.71-0.8) | 0.61\* | (0.56-0.66) | 0.61\* | (0.55-0.67) | 0.65\* | (0.58-0.71) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.56\* | (2.21-2.97) | 1.65\* | (1.49-1.83) | 1.24\* | (1.13-1.37) | 1 | (0.9-1.11) | **Ref** |  | 1.07 | (0.96-1.18) |
|  | ***Age<65 (N=21,851)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **5** | *Unadjusted odds ratio, (95% CI)* |  | |  | | | | 1.54\* | (1.29-1.84) | **Ref** |  | 0.84\* | (0.73-0.95) | 0.73\* | (0.64-0.85) | 0.69\* | (0.59-0.81) | 0.72\* | (0.62-0.84) |
|  | *Unadjusted odds ratio, (95% CI)* |  | |  | | | | 2.23\* | (1.78-2.79) | 1.45\* | (1.23-1.71) | 1.21\* | (1.05-1.4) | 1.06 | (0.93-1.21) | **Ref** |  | 1.05 | (0.89-1.23) |
| **6** | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 1.74\* | (1.46-2.07) | **Ref** |  | 0.77\* | (0.68-0.87) | 0.67\* | (0.58-0.78) | 0.64\* | (0.54-0.76) | 0.73\* | (0.63-0.84) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 2.71\* | (2.21-3.33) | 1.56\* | (1.32-1.85) | 1.19\* | (1.04-1.37) | 1.05 | (0.92-1.19) | **Ref** |  | 1.13 | (0.97-1.32) |
|  | ***Age>=65 (N=33,187)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **7** | *Unadjusted odds ratio, (95% CI)* |  | | | |  | | 1.45\* | (1.32-1.59) | **Ref** |  | 0.75\* | (0.7-0.8) | 0.62\* | (0.57-0.67) | 0.61\* | (0.55-0.67) | 0.57\* | (0.5-0.64) |
|  | *Unadjusted odds ratio, (95% CI)* |  | | | |  | | 2.39\* | (2.12-2.69) | 1.65\* | (1.49-1.83) | 1.24\* | (1.12-1.36) | 1.02 | (0.93-1.12) | **Ref** |  | 0.94 | (0.82-1.08) |
| **8** | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 1.58\* | (1.44-1.73) | **Ref** |  | 0.72\* | (0.68-0.77) | 0.6\* | (0.55-0.64) | 0.61\* | (0.55-0.67) | 0.6\* | (0.53-0.68) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 2.61\* | (2.3-2.95) | 1.65\* | (1.5-1.82) | 1.19\* | (1.08-1.32) | 0.98 | (0.88-1.09) | **Ref** |  | 0.99 | (0.87-1.13) |
|  | ***Age<=45 (N=5,702)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **8.1** | *Unadjusted odds ratio, (95% CI)* |  | | | |  | | 1.54\* | (1.12-2.12) | **Ref** |  | 0.99 | (0.76-1.28) | 0.64\* | (0.45-0.91) | 0.96 | (0.69-1.35) | 0.91 | (0.7-1.19) |
|  | *Unadjusted odds ratio, (95% CI)* |  | | | |  | | 1.6\* | (1.06-2.4) | 1.04 | (0.74-1.45) | 1.03 | (0.74-1.42) | 0.66\* | (0.45-0.99) | **Ref** |  | 0.95 | (0.62-1.43) |
| **8.1\_1** | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 1.76\* | (1.34-2.33) | **Ref** |  | 0.86 | (0.64-1.14) | 0.51\* | (0.34-0.76) | 0.82 | (0.59-1.13) | 0.88 | (0.65-1.18) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 2.16\* | (1.5-3.11) | 1.22 | (0.89-1.69) | 1.05 | (0.76-1.44) | 0.63\* | (0.44-0.9) | **Ref** |  | 1.07 | (0.71-1.63) |
|  | ***Age>45 (N=49,336)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **8.1\_2** | *Unadjusted odds ratio, (95% CI)* |  | | | |  | | 1.45\* | (1.34-1.57) | **Ref** |  | 0.75\* | (0.71-0.78) | 0.63\* | (0.58-0.67) | 0.57\* | (0.52-0.63) | 0.55\* | (0.49-0.61) |
|  | *Unadjusted odds ratio, (95% CI)* |  | | | |  | | 2.54\* | (2.23-2.89) | 1.75\* | (1.59-1.93) | 1.31\* | (1.19-1.44) | 1.09 | (1-1.2) | **Ref** |  | 0.96 | (0.87-1.05) |
| **8.1\_3** | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 1.62\* | (1.5-1.75) | **Ref** |  | 0.72\* | (0.69-0.76) | 0.62\* | (0.58-0.66) | 0.59\* | (0.54-0.65) | 0.63\* | (0.57-0.69) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 2.73\* | (2.41-3.08) | 1.68\* | (1.53-1.85) | 1.22\* | (1.11-1.34) | 1.04 | (0.94-1.16) | **Ref** |  | 1.06 | (0.96-1.16) |
|  | ***Age<=55 (N=12,393)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **8.2** | *Unadjusted odds ratio, (95% CI)* |  |  | | | | | 1.59\* | (1.32-1.92) | **Ref** |  | 0.91 | (0.79-1.05) | 0.78\* | (0.65-0.93) | 0.83 | (0.67-1.03) | 0.82 | (0.66-1.01) |
|  | *Unadjusted odds ratio, (95% CI)* |  |  | | | | | 1.91\* | (1.48-2.47) | 1.2 | (0.97-1.49) | 1.1 | (0.89-1.35) | 0.93 | (0.76-1.14) | **Ref** |  | 0.98 | (0.79-1.22) |
| **8.3** | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 1.78\* | (1.45-2.18) | **Ref** |  | 0.79\* | (0.68-0.92) | 0.67\* | (0.55-0.8) | 0.76\* | (0.6-0.95) | 0.78\* | (0.63-0.98) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 2.35\* | (1.83-3.02) | 1.32\* | (1.05-1.66) | 1.05 | (0.84-1.31) | 0.88 | (0.72-1.07) | **Ref** |  | 1.03 | (0.82-1.3) |
|  | ***Age>55 (N=42,645)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **8.3\_1** | *Unadjusted odds ratio, (95% CI)* |  | | | |  | | 1.44\* | (1.33-1.57) | **Ref** |  | 0.74\* | (0.71-0.78) | 0.61\* | (0.57-0.66) | 0.57\* | (0.52-0.62) | 0.54\* | (0.48-0.6) |
|  | *Unadjusted odds ratio, (95% CI)* |  | | | |  | | 2.54\* | (2.25-2.86) | 1.76\* | (1.61-1.92) | 1.3\* | (1.19-1.43) | 1.08 | (0.98-1.19) | **Ref** |  | 0.95 | (0.86-1.05) |
| **8.3\_2** | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 1.6\* | (1.47-1.74) | **Ref** |  | 0.72\* | (0.69-0.76) | 0.61\* | (0.57-0.65) | 0.58\* | (0.54-0.64) | 0.62\* | (0.56-0.68) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 2.74\* | (2.43-3.09) | 1.71\* | (1.57-1.87) | 1.24\* | (1.13-1.36) | 1.04 | (0.94-1.16) | **Ref** |  | 1.06 | (0.96-1.16) |
|  | ***Age<=35 (N=2,736)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **8.4** | *Unadjusted odds ratio, (95% CI)* |  | | | | |  | 1.17 | (0.76-1.8) | **Ref** |  | 0.91 | (0.67-1.25) | 0.37\* | (0.24-0.57) | 0.83 | (0.51-1.36) | 0.87 | (0.58-1.28) |
|  | *Unadjusted odds ratio, (95% CI)* |  | | | | |  | 1.41 | (0.83-2.41) | 1.2 | (0.73-1.97) | 1.1 | (0.6-2.01) | 0.45\* | (0.22-0.94) | **Ref** |  | 1.04 | (0.57-1.89) |
| **8.5** | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 1.38 | (0.87-2.2) | **Ref** |  | 0.82 | (0.58-1.15) | 0.3\* | (0.19-0.48) | 0.62 | (0.36-1.06) | 0.88 | (0.58-1.34) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 2.25\* | (1.21-4.18) | 1.63 | (0.94-2.81) | 1.33 | (0.7-2.51) | 0.49 | (0.23-1.04) | **Ref** |  | 1.44 | (0.77-2.67) |
|  | ***35<Age<=45 (N=2,966)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **8.6** | *Unadjusted odds ratio, (95% CI)* |  | | | | |  | 2.02\* | (1.3-3.13) | **Ref** |  | 0.98 | (0.7-1.37) | 0.78 | (0.5-1.23) | 0.99 | (0.68-1.45) | 0.87 | (0.62-1.2) |
|  | *Unadjusted odds ratio, (95% CI)* |  | | | | |  | 2.04\* | (1.16-3.58) | 1.01 | (0.69-1.47) | 0.99 | (0.69-1.41) | 0.79 | (0.5-1.23) | **Ref** |  | 0.87 | (0.57-1.34) |
| **8.7** | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 2.22\* | (1.47-3.34) | **Ref** |  | 0.9 | (0.64-1.28) | 0.67 | (0.41-1.1) | 0.94 | (0.63-1.4) | 0.92 | (0.6-1.41) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 2.35\* | (1.34-4.14) | 1.06 | (0.71-1.58) | 0.96 | (0.66-1.39) | 0.71 | (0.45-1.13) | **Ref** |  | 0.97 | (0.6-1.58) |
|  | ***45<Age<=55 (N=6,691)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **8.8** | *Unadjusted odds ratio, (95% CI)* |  | | | |  | | 1.59\* | (1.28-1.96) | **Ref** |  | 0.83 | (0.68-1.01) | 0.81\* | (0.66-0.99) | 0.72\* | (0.53-0.96) | 0.73\* | (0.55-0.97) |
|  | *Unadjusted odds ratio, (95% CI)* |  | | | |  | | 2.21\* | (1.63-3) | 1.4\* | (1.04-1.88) | 1.16 | (0.91-1.47) | 1.13 | (0.88-1.44) | **Ref** |  | 1.02 | (0.81-1.29) |
| **8.9** | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 1.8\* | (1.41-2.31) | **Ref** |  | 0.75\* | (0.63-0.91) | 0.73\* | (0.59-0.91) | 0.71\* | (0.52-0.96) | 0.71\* | (0.53-0.96) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 2.55\* | (1.88-3.46) | 1.41\* | (1.04-1.93) | 1.07 | (0.83-1.37) | 1.04 | (0.81-1.33) | **Ref** |  | 1.01 | (0.78-1.3) |
|  | ***55<Age<=65 (N=10,632)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **8.10** | *Unadjusted odds ratio, (95% CI)* |  | | | |  | | 1.43\* | (1.13-1.81) | **Ref** |  | 0.72\* | (0.62-0.84) | 0.65\* | (0.55-0.77) | 0.56\* | (0.46-0.67) | 0.65\* | (0.55-0.76) |
|  | *Unadjusted odds ratio, (95% CI)* |  | | | |  | | 2.58\* | (1.98-3.35) | 1.8\* | (1.5-2.17) | 1.3\* | (1.08-1.56) | 1.18 | (0.98-1.41) | **Ref** |  | 1.17 | (0.98-1.39) |
| **8.11** | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 1.62\* | (1.26-2.09) | **Ref** |  | 0.7\* | (0.61-0.82) | 0.63\* | (0.53-0.74) | 0.53\* | (0.44-0.63) | 0.67\* | (0.57-0.79) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 3.08\* | (2.32-4.09) | 1.9\* | (1.59-2.27) | 1.34\* | (1.13-1.58) | 1.19 | (0.98-1.44) | **Ref** |  | 1.27 | (1.07-1.52) |
|  | ***65<Age<=75 (N=12,124)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **8.12** | *Unadjusted odds ratio, (95% CI)* |  | | |  | | | 1.33\* | (1.15-1.54) | **Ref** |  | 0.7\* | (0.63-0.79) | 0.66\* | (0.57-0.77) | 0.65\* | (0.56-0.76) | 0.56\* | (0.45-0.68) |
|  | *Unadjusted odds ratio, (95% CI)* |  | | |  | | | 2.04\* | (1.67-2.48) | 1.53\* | (1.31-1.78) | 1.07 | (0.93-1.24) | 1.01 | (0.87-1.19) | **Ref** |  | 0.85 | (0.71-1.01) |
| **8.13** | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 1.48\* | (1.29-1.71) | **Ref** |  | 0.65\* | (0.58-0.73) | 0.59\* | (0.51-0.69) | 0.59\* | (0.5-0.7) | 0.51\* | (0.42-0.61) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 2.5\* | (2.01-3.11) | 1.69\* | (1.43-1.98) | 1.09 | (0.94-1.28) | 1 | (0.85-1.18) | **Ref** |  | 0.86 | (0.72-1.02) |
|  | ***75<Age (N=19,889)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **8.14** | *Unadjusted odds ratio, (95% CI)* |  | |  | | | | 1.52\* | (1.35-1.71) | **Ref** |  | 0.79\* | (0.74-0.86) | 0.63\* | (0.56-0.7) | 0.62\* | (0.54-0.72) | 0.66\* | (0.55-0.79) |
|  | *Unadjusted odds ratio, (95% CI)* |  | |  | | | | 2.45\* | (2.06-2.91) | 1.61\* | (1.4-1.87) | 1.28\* | (1.11-1.48) | 1.01 | (0.88-1.17) | **Ref** |  | 1.06 | (0.85-1.33) |
| **8.15** | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 1.63\* | (1.44-1.85) | **Ref** |  | 0.77\* | (0.71-0.83) | 0.6\* | (0.54-0.66) | 0.61\* | (0.53-0.71) | 0.68\* | (0.57-0.82) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Sofa & Elix Score | | | | | | 2.68\* | (2.23-3.21) | 1.64\* | (1.42-1.9) | 1.26\* | (1.1-1.45) | 0.99 | (0.85-1.14) | **Ref** |  | 1.12 | (0.9-1.38) |
|  | ***Without 2015 (ref="2014") (N=47,390)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **9** | *Unadjusted odds ratio, (95% CI)* |  | |  | | | | 1.5\* | (1.39-1.63) | **Ref** |  | 0.77\* | (0.72-0.81) | 0.62\* | (0.57-0.68) | 0.59\* | (0.53-0.65) | 0.54\* | (0.48-0.6) |
|  | *Unadjusted odds ratio, (95% CI)* |  | |  | | | | 2.56\* | (2.23-2.94) | 1.7\* | (1.53-1.88) | 1.3\* | (1.18-1.44) | 1.06 | (0.95-1.18) | **Ref** |  | 0.91 | (0.82-1.01) |
| **10** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.62\* | (1.5-1.75) | **Ref** |  | 0.74\* | (0.7-0.79) | 0.62\* | (0.58-0.68) | 0.62\* | (0.56-0.68) | 0.65\* | (0.59-0.71) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.61\* | (2.3-2.96) | 1.61\* | (1.47-1.77) | 1.2\* | (1.1-1.32) | 1.01 | (0.91-1.12) | **Ref** |  | 1.05 | (0.95-1.16) |
|  | ***With Cont. Albumin (N=41,312)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **11** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.47\* | (1.35-1.6) | **Ref** |  | 0.78\* | (0.73-0.82) | 0.68\* | (0.63-0.74) | 0.67\* | (0.61-0.74) | 0.72\* | (0.66-0.79) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.18\* | (1.93-2.46) | 1.49\* | (1.35-1.64) | 1.15\* | (1.04-1.28) | 1.01 | (0.92-1.11) | **Ref** |  | 1.07 | (0.97-1.19) |
|  | ***With Cont. Albumin 0-2 (N=2,785)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **12** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.23\* | (0.95-1.59) | **Ref** |  | 0.69\* | (0.55-0.87) | 0.76\* | (0.61-0.94) | 0.86 | (0.6-1.24) | 1.04 | (0.76-1.42) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.43 | (0.96-2.14) | 1.16 | (0.81-1.67) | 0.8 | (0.58-1.11) | 0.88 | (0.62-1.25) | **Ref** |  | 1.21 | (0.76-1.91) |
|  | ***With Cont. Albumin 2-3 (N=14,199)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **13** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.52\* | (1.32-1.76) | **Ref** |  | 0.84\* | (0.78-0.92) | 0.73\* | (0.64-0.82) | 0.6\* | (0.52-0.69) | 0.66\* | (0.56-0.77) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.55\* | (2.16-3.01) | 1.68\* | (1.46-1.92) | 1.42\* | (1.23-1.63) | 1.22\* | (1.07-1.39) | **Ref** |  | 1.1 | (0.96-1.26) |
|  | ***With Cont. Albumin 3+ (N=24,328)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **14** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.46\* | (1.25-1.7) | **Ref** |  | 0.73\* | (0.67-0.8) | 0.63\* | (0.56-0.7) | 0.72\* | (0.63-0.84) | 0.74\* | (0.63-0.87) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.01\* | (1.62-2.5) | 1.38\* | (1.19-1.6) | 1.01 | (0.86-1.18) | 0.86 | (0.75-1) | **Ref** |  | 1.02 | (0.86-1.21) |
|  | ***With icu=Yes and icu\_category (ref="medical") (N=14,511)*** | | | | | | | | | | |  |  |  |  |  |  |  |  |
| **15** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.36\* | (1.18-1.58) | **Ref** |  | 0.78\* | (0.71-0.85) | 0.68\* | (0.6-0.77) | 0.64\* | (0.55-0.74) | 0.8\* | (0.71-0.89) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.13\* | (1.73-2.62) | 1.56\* | (1.35-1.81) | 1.22\* | (1.05-1.41) | 1.06 | (0.9-1.24) | **Ref** |  | 1.24\* | (1.05-1.48) |
|  | ***Septic Shock=Yes (N=6,875)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **16** | *Unadjusted odds ratio, (95% CI)* |  | | | | |  | 1.54\* | (1.22-1.94) | **Ref** |  | 0.84\* | (0.72-0.98) | 0.82\* | (0.69-0.98) | 0.75\* | (0.61-0.93) | 0.71\* | (0.61-0.83) |
|  | *Unadjusted odds ratio, (95% CI)* |  | | | | |  | 2.04\* | (1.56-2.68) | 1.33\* | (1.08-1.63) | 1.12 | (0.88-1.44) | 1.09 | (0.92-1.31) | **Ref** |  | 0.94 | (0.75-1.18) |
| **17** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.58\* | (1.26-2) | **Ref** |  | 0.83\* | (0.72-0.96) | 0.8\* | (0.67-0.95) | 0.77\* | (0.62-0.97) | 0.81\* | (0.68-0.96) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.05\* | (1.6-2.63) | 1.29\* | (1.04-1.62) | 1.07 | (0.82-1.4) | 1.03 | (0.86-1.24) | **Ref** |  | 1.05 | (0.83-1.32) |
|  | ***with only CardPulm sofa\_score*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **18** | *Adjusted odds ratio, (95% CI)* | With Cont. Age & Sofa Score | | | | | | 1.54\* | (1.43-1.66) | **Ref** |  | 0.74\* | (0.7-0.77) | 0.62\* | (0.58-0.67) | 0.61\* | (0.56-0.66) | 0.63\* | (0.58-0.69) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Age and Sofa Score | | | | | | 2.54\* | (2.25-2.86) | 1.65\* | (1.51-1.8) | 1.21\* | (1.11-1.32) | 1.02 | (0.93-1.12) | **Ref** |  | 1.03 | (0.95-1.13) |
|  | ***with only cardiovascular sofa\_score*** | | | | | | | | | | |  |  |  |  |  |  |  |  |
| **19.1** | *Adjusted odds ratio, (95% CI)* | With Cont. Age & Sofa Score | | | | | | 1.54\* | (1.42-1.66) | **Ref** |  | 0.75\* | (0.71-0.78) | 0.64\* | (0.6-0.68) | 0.63\* | (0.58-0.69) | 0.66\* | (0.61-0.72) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Age and Sofa Score | | | | | | 2.43\* | (2.16-2.73) | 1.58\* | (1.45-1.72) | 1.18\* | (1.09-1.28) | 1.01 | (0.92-1.1) | **Ref** |  | 1.05 | (0.97-1.14) |
|  | ***with only coagulation sofa\_score*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **19.2** | *Adjusted odds ratio, (95% CI)* | With Cont. Age & Sofa Score | | | | | | 1.57\* | (1.45-1.69) | **Ref** |  | 0.75\* | (0.72-0.79) | 0.65\* | (0.61-0.69) | 0.65\* | (0.6-0.71) | 0.71\* | (0.64-0.77) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Age and Sofa Score | | | | | | 2.41\* | (2.14-2.71) | 1.54\* | (1.42-1.67) | 1.16\* | (1.07-1.26) | 1 | (0.92-1.08) | **Ref** |  | 1.08\* | (1-1.17) |
|  | ***with only gcs sofa\_score*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **19.3** | *Adjusted odds ratio, (95% CI)* | With Cont. Age & Sofa Score | | | | | | 1.52\* | (1.41-1.64) | **Ref** |  | 0.76\* | (0.72-0.79) | 0.65\* | (0.61-0.7) | 0.65\* | (0.6-0.71) | 0.7\* | (0.64-0.76) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Age and Sofa Score | | | | | | 2.33\* | (2.07-2.62) | 1.53\* | (1.41-1.67) | 1.16\* | (1.06-1.27) | 1 | (0.91-1.1) | **Ref** |  | 1.07 | (0.98-1.17) |
|  | ***with only hepatic sofa\_score*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **19.4** | *Adjusted odds ratio, (95% CI)* | With Cont. Age & Sofa Score | | | | | | 1.58\* | (1.47-1.71) | **Ref** |  | 0.75\* | (0.71-0.78) | 0.64\* | (0.6-0.68) | 0.63\* | (0.59-0.69) | 0.69\* | (0.63-0.75) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Age and Sofa Score | | | | | | 2.5\* | (2.23-2.8) | 1.58\* | (1.46-1.71) | 1.18\* | (1.08-1.28) | 1 | (0.92-1.09) | **Ref** |  | 1.08 | (0.99-1.18) |
|  | ***with only renal sofa\_score*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **19.5** | *Adjusted odds ratio, (95% CI)* | With Cont. Age & Sofa Score | | | | | | 1.56\* | (1.44-1.68) | **Ref** |  | 0.75\* | (0.71-0.78) | 0.63\* | (0.59-0.67) | 0.62\* | (0.57-0.68) | 0.67\* | (0.61-0.73) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Age and Sofa Score | | | | | | 2.5\* | (2.22-2.82) | 1.6\* | (1.48-1.74) | 1.2\* | (1.1-1.3) | 1.01 | (0.93-1.1) | **Ref** |  | 1.07 | (0.98-1.16) |
|  | ***with only pulmonary sofa\_score*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **19.6** | *Adjusted odds ratio, (95% CI)* | With Cont. Age & Sofa Score | | | | | | 1.54\* | (1.42-1.66) | **Ref** |  | 0.74\* | (0.71-0.78) | 0.62\* | (0.58-0.67) | 0.61\* | (0.56-0.66) | 0.64\* | (0.58-0.7) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Age and Sofa Score | | | | | | 2.53\* | (2.24-2.85) | 1.64\* | (1.51-1.79) | 1.22\* | (1.12-1.33) | 1.03 | (0.94-1.12) | **Ref** |  | 1.05 | (0.96-1.14) |
|  | ***sofa\_score 0-2 (N=23,536)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **20** | *Adjusted odds ratio, (95% CI)* | With Cont. Age & Sofa Score | | | | | | 1.73\* | (1.5-1.98) | **Ref** |  | 0.67\* | (0.61-0.73) | 0.57\* | (0.51-0.64) | 0.5\* | (0.42-0.6) | 0.54\* | (0.46-0.63) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Age and Sofa Score | | | | | | 3.44\* | (2.78-4.26) | 1.99\* | (1.68-2.37) | 1.33\* | (1.13-1.56) | 1.13 | (0.93-1.39) | **Ref** |  | 1.08 | (0.91-1.28) |
|  | ***sofa\_score 3 (N=8,871)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **21** | *Adjusted odds ratio, (95% CI)* | With Cont. Age & Sofa Score | | | | | | 1.54\* | (1.22-1.93) | **Ref** |  | 0.72\* | (0.63-0.84) | 0.59\* | (0.49-0.71) | 0.53\* | (0.4-0.69) | 0.57\* | (0.45-0.74) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Age and Sofa Score | | | | | | 2.91\* | (2.22-3.81) | 1.9\* | (1.44-2.49) | 1.37\* | (1.05-1.79) | 1.12 | (0.81-1.54) | **Ref** |  | 1.09 | (0.83-1.43) |
|  | ***sofa\_score 4-5 (N=11,528)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **22** | *Adjusted odds ratio, (95% CI)* | With Cont. Age & Sofa Score | | | | | | 1.76\* | (1.48-2.1) | **Ref** |  | 0.78\* | (0.69-0.88) | 0.64\* | (0.56-0.74) | 0.64\* | (0.54-0.76) | 0.66\* | (0.53-0.82) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Age and Sofa Score | | | | | | 2.76\* | (2.2-3.46) | 1.57\* | (1.32-1.85) | 1.23\* | (1.02-1.47) | 1.01 | (0.84-1.21) | **Ref** |  | 1.04 | (0.81-1.34) |
|  | ***sofa\_score 6+ (N=11,103)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **23** | *Adjusted odds ratio, (95% CI)* | With Cont. Age & Sofa Score | | | | | | 1.38\* | (1.12-1.7) | **Ref** |  | 0.77\* | (0.69-0.85) | 0.65\* | (0.55-0.76) | 0.74\* | (0.62-0.88) | 0.77\* | (0.66-0.9) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont. Age and Sofa Score | | | | | | 1.88\* | (1.57-2.23) | 1.36\* | (1.14-1.62) | 1.04 | (0.9-1.2) | 0.88 | (0.74-1.05) | **Ref** |  | 1.05 | (0.87-1.26) |
|  | ***gender=Female (N=27,390)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **24** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.42\* | (1.29-1.58) | **Ref** |  | 0.77\* | (0.71-0.84) | 0.62\* | (0.55-0.68) | 0.61\* | (0.54-0.68) | 0.66\* | (0.59-0.74) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.34\* | (2.03-2.7) | 1.64\* | (1.47-1.84) | 1.27\* | (1.12-1.44) | 1.01 | (0.89-1.15) | **Ref** |  | 1.08 | (0.96-1.22) |
|  | ***gender=Male (N=27,648)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **25** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.81\* | (1.61-2.02) | **Ref** |  | 0.72\* | (0.67-0.77) | 0.62\* | (0.57-0.68) | 0.62\* | (0.55-0.7) | 0.65\* | (0.57-0.76) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.91\* | (2.44-3.48) | 1.61\* | (1.42-1.83) | 1.16\* | (1.03-1.3) | 1 | (0.89-1.13) | **Ref** |  | 1.06 | (0.89-1.25) |
|  | ***race=Black (N=10,062)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **26** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.63\* | (1.38-1.93) | **Ref** |  | 0.78\* | (0.71-0.86) | 0.79\* | (0.65-0.96) | 0.58\* | (0.48-0.7) | 0.74\* | (0.62-0.88) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.81\* | (2.08-3.79) | 1.72\* | (1.43-2.07) | 1.35\* | (1.09-1.66) | 1.36\* | (1.07-1.73) | **Ref** |  | 1.27 | (0.99-1.63) |
|  | ***race=White (N=41,671)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **27** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.58\* | (1.45-1.71) | **Ref** |  | 0.74\* | (0.7-0.79) | 0.59\* | (0.55-0.63) | 0.62\* | (0.56-0.68) | 0.63\* | (0.58-0.7) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.56\* | (2.26-2.88) | 1.62\* | (1.47-1.78) | 1.2\* | (1.1-1.32) | 0.96 | (0.87-1.05) | **Ref** |  | 1.03 | (0.93-1.13) |
|  | ***Site of Infection=intra-abdominal (N=4,220)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **28.1** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.39 | (0.97-1.98) | **Ref** |  | 0.69\* | (0.55-0.86) | 0.7\* | (0.53-0.92) | 0.83 | (0.59-1.16) | 0.56\* | (0.39-0.8) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.68\* | (1.03-2.74) | 1.21 | (0.86-1.7) | 0.83 | (0.63-1.1) | 0.84 | (0.62-1.14) | **Ref** |  | 0.68\* | (0.46-0.98) |
|  | ***Site of Infection=multiple site (N=8,208)*** | | | | | | | | | | | | | | |  | |  |  |
| **28.2** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.52\* | (1.19-1.94) | **Ref** |  | 0.66\* | (0.59-0.74) | 0.57\* | (0.47-0.68) | 0.58\* | (0.46-0.74) | 0.65\* | (0.49-0.85) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.61\* | (1.95-3.49) | 1.71\* | (1.35-2.17) | 1.14 | (0.91-1.41) | 0.98 | (0.75-1.27) | **Ref** |  | 1.11 | (0.81-1.51) |
|  | ***Site of Infection=pneumonia (N=13,560)*** | | | | | | |  |  |  |  |  |  |  |  |  |  |  |  |
| **28.3** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.64\* | (1.38-1.95) | **Ref** |  | 0.7\* | (0.62-0.78) | 0.56\* | (0.5-0.64) | 0.45\* | (0.37-0.53) | 0.53\* | (0.43-0.66) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 3.67\* | (2.91-4.61) | 2.24\* | (1.88-2.67) | 1.56\* | (1.28-1.9) | 1.26\* | (1.04-1.52) | **Ref** |  | 1.19 | (0.93-1.52) |
|  | ***Site of Infection=septicemia-bacteremia NEC (N=4,249)*** | | | | | | |  |  |  |  |  |  |  |  |  |  |  |  |
| **28.4** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.69\* | (1.34-2.12) | **Ref** |  | 0.83\* | (0.71-0.98) | 0.94 | (0.75-1.17) | 0.78\* | (0.62-0.99) | 0.79 | (0.59-1.06) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.16\* | (1.66-2.8) | 1.28\* | (1.01-1.62) | 1.07 | (0.79-1.43) | 1.2 | (0.91-1.58) | **Ref** |  | 1.02 | (0.76-1.36) |
|  | ***Site of Infection=soft-tissue infection (N=3,001)*** | | | | | | |  |  |  |  |  |  |  |  |  |  |  |  |
| **28.5** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 0.82 | (0.39-1.76) | **Ref** |  | 0.54\* | (0.33-0.86) | 0.52\* | (0.32-0.83) | 0.66 | (0.43-1.02) | 0.78 | (0.53-1.14) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.24 | (0.65-2.35) | 1.5 | (0.98-2.31) | 0.81 | (0.48-1.36) | 0.78 | (0.46-1.31) | **Ref** |  | 1.17 | (0.69-1.98) |
|  | ***Site of Infection=unspecified (N=12,951)*** | | | | | | |  |  |  |  |  |  |  |  |  |  |  |  |
| **28.6** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.75\* | (1.45-2.11) | **Ref** |  | 0.84\* | (0.75-0.94) | 0.63\* | (0.55-0.71) | 0.67\* | (0.56-0.82) | 0.67\* | (0.57-0.8) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.59\* | (2-3.36) | 1.48\* | (1.23-1.79) | 1.24\* | (1.02-1.51) | 0.93 | (0.73-1.18) | **Ref** |  | 1 | (0.81-1.24) |
|  | ***Site of Infection=uti (N=8,849)*** | | | | | | |  |  |  |  |  |  |  |  |  |  |  |  |
| **28.7** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.36\* | (1.2-1.56) | **Ref** |  | 0.73\* | (0.63-0.84) | 0.54\* | (0.43-0.67) | 0.57\* | (0.45-0.73) | 0.68\* | (0.54-0.86) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.39\* | (1.86-3.08) | 1.75\* | (1.38-2.23) | 1.27 | (0.99-1.63) | 0.94 | (0.72-1.23) | **Ref** |  | 1.19 | (0.88-1.61) |
|  | ***Abx administration = -2 (N=2,580)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **30** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.78\* | (1.18-2.67) | **Ref** |  | 0.93 | (0.74-1.17) | 0.66\* | (0.47-0.93) | 0.56\* | (0.36-0.86) | 0.7 | (0.48-1.03) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 3.19\* | (1.97-5.17) | 1.79\* | (1.16-2.78) | 1.67\* | (1.13-2.47) | 1.19 | (0.75-1.89) | **Ref** |  | 1.26 | (0.79-2.01) |
|  | ***Abx administration = -1 (N=4,552)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **31** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.39 | (0.96-1.99) | **Ref** |  | 0.71\* | (0.61-0.83) | 0.61\* | (0.51-0.73) | 0.56\* | (0.42-0.76) | 0.81 | (0.61-1.08) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.46\* | (1.57-3.86) | 1.78\* | (1.32-2.39) | 1.26 | (0.95-1.67) | 1.08 | (0.78-1.5) | **Ref** |  | 1.44 | (0.96-2.17) |
|  | ***Abx administration = 0 (N=40,167)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **32** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.64\* | (1.48-1.81) | **Ref** |  | 0.73\* | (0.69-0.77) | 0.59\* | (0.55-0.64) | 0.59\* | (0.53-0.66) | 0.62\* | (0.56-0.69) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.76\* | (2.39-3.18) | 1.68\* | (1.51-1.88) | 1.23\* | (1.1-1.37) | 1 | (0.89-1.12) | **Ref** |  | 1.04 | (0.91-1.18) |
|  | ***Abx administration = 0 (N=random sample of 2,274)*** | | | | | | | | | | | | | | | | | | |
| **32.1** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.97\* | (1.42-2.73) | **Ref** |  | 0.67\* | (0.48-0.92) | 0.72 | (0.48-1.08) | 0.6 | (0.34-1.07) | 0.52\* | (0.31-0.89) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 3.28\* | (1.86-5.78) | 1.67 | (0.93-2.98) | 1.11 | (0.57-2.17) | 1.2 | (0.65-2.22) | **Ref** |  | 0.87 | (0.43-1.76) |
|  | ***Abx administration = 1 (N=5,465)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **33** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.49\* | (1.21-1.84) | **Ref** |  | 0.75\* | (0.64-0.88) | 0.67\* | (0.55-0.83) | 0.81 | (0.62-1.06) | 0.76 | (0.58-1) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.83\* | (1.29-2.6) | 1.23 | (0.94-1.61) | 0.92 | (0.72-1.18) | 0.83 | (0.62-1.1) | **Ref** |  | 0.94 | (0.67-1.31) |
|  | ***Abx administration = 2 (N=2,274)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **34** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.11 | (0.72-1.7) | **Ref** |  | 0.8\* | (0.65-0.99) | 0.92 | (0.69-1.22) | 0.71\* | (0.51-0.99) | 0.85 | (0.51-1.42) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.55\* | (1.02-2.37) | 1.4\* | (1.01-1.95) | 1.12 | (0.79-1.6) | 1.29 | (0.9-1.84) | **Ref** |  | 1.19 | (0.66-2.16) |
|  | ***Elixhauser Score = 0-2 (N=13,109)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **35** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.44\* | (1.11-1.87) | **Ref** |  | 0.72\* | (0.61-0.84) | 0.55\* | (0.47-0.65) | 0.53\* | (0.41-0.68) | 0.71\* | (0.57-0.88) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.71\* | (1.98-3.71) | 1.89\* | (1.47-2.43) | 1.35\* | (1.08-1.7) | 1.04 | (0.8-1.36) | **Ref** |  | 1.35 | (0.95-1.9) |
|  | ***Elixhauser Score = 3 (N=9,046)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **36** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.49\* | (1.21-1.83) | **Ref** |  | 0.64\* | (0.56-0.72) | 0.62\* | (0.5-0.77) | 0.66\* | (0.5-0.88) | 0.62\* | (0.51-0.76) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.24\* | (1.57-3.2) | 1.51\* | (1.14-1.99) | 0.96 | (0.71-1.28) | 0.94 | (0.69-1.28) | **Ref** |  | 0.93 | (0.72-1.21) |
|  | ***Elixhauser Score = 4-5 (N=17,806)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **37** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.71\* | (1.46-2.01) | **Ref** |  | 0.75\* | (0.67-0.82) | 0.62\* | (0.56-0.69) | 0.59\* | (0.51-0.68) | 0.63\* | (0.53-0.75) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.91\* | (2.35-3.6) | 1.7\* | (1.47-1.96) | 1.26\* | (1.07-1.49) | 1.06 | (0.9-1.24) | **Ref** |  | 1.07 | (0.88-1.31) |
|  | ***Elixhauser Score = 6+ (N=15,077)*** | | | | | | | | |  |  |  |  |  |  |  |  |  |  |
| **38** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.55\* | (1.34-1.8) | **Ref** |  | 0.79\* | (0.72-0.87) | 0.65\* | (0.58-0.74) | 0.66\* | (0.57-0.77) | 0.64\* | (0.55-0.76) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.34\* | (2.01-2.72) | 1.51\* | (1.3-1.74) | 1.2\* | (1.06-1.35) | 0.98 | (0.89-1.1) | **Ref** |  | 0.97 | (0.82-1.15) |
|  | ***Congestive heart failure: Elixhauser group 1 alone (N=15,729)*** | | | | | | | | | | | | | | | | | | |
| **39** | *Adjusted odds ratio, (95% CI)* | With Cont Age & Sofa Score | | | | | | 1.48\* | (1.28-1.7) | **Ref** |  | 0.78\* | (0.72-0.84) | 0.63\* | (0.56-0.7) | 0.67\* | (0.6-0.76) | 0.63\* | (0.53-0.74) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont Age & Sofa Score | | | | | | 2.19\* | (1.86-2.59) | 1.48\* | (1.32-1.67) | 1.15\* | (1.01-1.32) | 0.93 | (0.82-1.05) | **Ref** |  | 0.93 | (0.78-1.12) |
|  | ***Hypertension: Elixhauser groups 6 and 7 combined (N=34,680)*** | | | | | | | | | | | | | | | | | | |
| **40** | *Adjusted odds ratio, (95% CI)* | With Cont Age & Sofa Score | | | | | | 1.64\* | (1.47-1.83) | **Ref** |  | 0.76\* | (0.72-0.8) | 0.67\* | (0.61-0.72) | 0.62\* | (0.55-0.7) | 0.71\* | (0.63-0.8) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont Age & Sofa Score | | | | | | 2.63\* | (2.26-3.07) | 1.61\* | (1.43-1.81) | 1.22\* | (1.09-1.37) | 1.07 | (0.95-1.2) | **Ref** |  | 1.14 | (1-1.29) |
|  | ***Chronic pulmonary disease: Elixhauser group 10 alone (N=20,015)*** | | | | | | | | | | | | | | | | | | |
| **41** | *Adjusted odds ratio, (95% CI)* | With Cont Age & Sofa Score | | | | | | 1.75\* | (1.52-2.01) | **Ref** |  | 0.79\* | (0.71-0.89) | 0.63\* | (0.56-0.71) | 0.63\* | (0.55-0.73) | 0.65\* | (0.57-0.75) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont Age & Sofa Score | | | | | | 2.77\* | (2.38-3.23) | 1.58\* | (1.37-1.82) | 1.25\* | (1.08-1.45) | 0.99 | (0.86-1.15) | **Ref** |  | 1.03 | (0.89-1.21) |
|  | ***Diabetes: Elixhauser groups 11 and 12 combined (N=18,473)*** | | | | | | | | | | | | | | | | | | |
| **42** | *Adjusted odds ratio, (95% CI)* | With Cont Age & Sofa Score | | | | | | 1.65\* | (1.4-1.95) | **Ref** |  | 0.77\* | (0.71-0.83) | 0.62\* | (0.56-0.69) | 0.67\* | (0.57-0.79) | 0.7\* | (0.61-0.81) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont Age & Sofa Score | | | | | | 2.46\* | (2-3.03) | 1.49\* | (1.27-1.75) | 1.15 | (0.99-1.33) | 0.93 | (0.79-1.09) | **Ref** |  | 1.04 | (0.89-1.22) |
|  | ***Cancer: Elixhauser groups 18 and 19 and 20 combined (N=6,669)*** | | | | | | | | | | | | | | | | | | |
| **43** | *Adjusted odds ratio, (95% CI)* | With Cont Age & Sofa Score | | | | | | 1.56\* | (1.28-1.88) | **Ref** |  | 0.68\* | (0.59-0.79) | 0.7\* | (0.6-0.81) | 0.7\* | (0.55-0.88) | 0.6\* | (0.48-0.74) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont Age & Sofa Score | | | | | | 2.23\* | (1.75-2.85) | 1.44\* | (1.14-1.81) | 0.98 | (0.8-1.2) | 1 | (0.82-1.23) | **Ref** |  | 0.86 | (0.63-1.17) |
|  | ***Weight loss: Elixhauser group 24 alone (N=7,466)*** | | | | | | | | | | | | | | | | | | |
| **44** | *Adjusted odds ratio, (95% CI)* | With Cont Age & Sofa Score | | | | | | 1.34\* | (1.15-1.56) | **Ref** |  | 0.87 | (0.76-1) | 0.75\* | (0.65-0.86) | 0.69\* | (0.54-0.89) | 0.64\* | (0.46-0.9) |
|  | *Adjusted odds ratio, (95% CI)* | With Cont Age & Sofa Score | | | | | | 1.93\* | (1.51-2.47) | 1.44\* | (1.13-1.85) | 1.26\* | (1.02-1.55) | 1.08 | (0.86-1.37) | **Ref** |  | 0.93 | (0.7-1.24) |
|  | ***Explicit sepsis*** | | | | | | |  |  |  |  |  |  |  |  |  |  |  |  |
| **45.2** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.49\* | (1.33-1.67) | **Ref** |  | 0.77\* | (0.71-0.83) | 0.69\* | (0.62-0.78) | 0.69\* | (0.6-0.8) | 0.72\* | (0.63-0.82) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.16\* | (1.83-2.54) | 1.45\* | (1.26-1.67) | 1.12 | (0.96-1.3) | 1.01 | (0.89-1.14) | **Ref** |  | 1.04 | (0.9-1.21) |
|  | ***Explicit severe sepsis*** | | | | | | |  |  |  |  |  |  |  |  |  |  |  |  |
| **46.2** | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 1.55\* | (1.34-1.8) | **Ref** |  | 0.75\* | (0.68-0.83) | 0.71\* | (0.62-0.83) | 0.74\* | (0.62-0.88) | 0.72\* | (0.62-0.83) |
|  | *Adjusted odds ratio, (95% CI)* | With Categorical Age & Sofa Score | | | | | | 2.1\* | (1.76-2.51) | 1.36\* | (1.14-1.61) | 1.02 | (0.84-1.23) | 0.97 | (0.83-1.13) | **Ref** |  | 0.97 | (0.82-1.16) |
| Key:  Ref = BMI category that other BMI categories are compared to  \* p-value < 0.05 | | | | | | | | | | | | | | | | | | | |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Table E6. Baseline characteristics and outcomes of inpatients with gastrointestinal bleeds** | | | | | | | | | | | | | | | | | | | | |
|  | **All patients** | | **BMI categories** | | | | | | | | | | | |  |  | |  |  | | |
|  |  | | **Underweight** | | **Normal** | | **Overweight** | | **Obese Class I** | | **Obese Class II** | | **Obese Class III** | | **Data used in the Analysis** | | | **Data not used in the Analysis** | | |
| **Body Mass Index** |  | | **< 18.5 kg/m2** | | **18.5 - 24.9 kg/m2** | | **25.0 - 29.9 kg/m2** | | **30.0 - 34.9 kg/m2** | | **35.0 - 39.9 kg/m2** | | **> 40.0 kg/m2** | |  | | |  | | |
|  | (n=32,663) | | (n=1,234) | | (n=8,834) | | (n=7,897) | | (n=4,606) | | (n=2,072) | | (n=1,618) | | (n=26,261) | | | (n=6,402) | | |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  | |  |
| **Age in years, median (IQR)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  | |  |
|  | 69 | (55-80) | 73 | (59-85) | 73 | (57-84) | 70 | (57-81) | 67 | (55-77) | 65 | (53-74) | 62 | (52-71) | 69 | | (56-81) | 67 | | (52-80) |
| **Gender, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  | |  |
| *Male* | 16896 | (51.7) | 517 | (41.9) | 4484 | (50.8) | 4478 | (56.7) | 2466 | (53.5) | 909 | (43.9) | 622 | (38.4) | 13476 | | (51.3) | 3420 | | (53.4) |
| **Ethnicity, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  | |  |
| *Asian* | 577 | (1.8) | 42 | (3.4) | 236 | (2.7) | 146 | (1.8) | 41 | (0.9) | 9 | (0.4) | 6 | (0.4) | 480 | | (1.8) | 97 | | (1.5) |
| *Black* | 6378 | (19.5) | 313 | (25.4) | 1719 | (19.5) | 1453 | (18.4) | 852 | (18.5) | 448 | (21.6) | 391 | (24.2) | 5176 | | (19.7) | 1202 | | (18.8) |
| *Hispanic* | 284 | (0.9) | 6 | (0.5) | 65 | (0.7) | 87 | (1.1) | 43 | (0.9) | 12 | (0.6) | 16 | (1) | 229 | | (0.9) | 55 | | (0.9) |
| *Other* | 1261 | (3.9) | 36 | (2.9) | 296 | (3.4) | 336 | (4.3) | 199 | (4.3) | 86 | (4.2) | 66 | (4.1) | 1019 | | (3.9) | 242 | | (3.8) |
| *Unknown* | 505 | (1.5) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | | (0) | 505 | | (7.9) |
| *White* | 23658 | (72.4) | 837 | (67.8) | 6518 | (73.8) | 5875 | (74.4) | 3471 | (75.4) | 1517 | (73.2) | 1139 | (70.4) | 19357 | | (73.7) | 4301 | | (67.2) |
| **Admission year, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  | |  |
| *Pre-2010* | 1632 | (5) | 66 | (5.3) | 455 | (5.2) | 394 | (5) | 222 | (4.8) | 106 | (5.1) | 75 | (4.6) | 1318 | | (5) | 314 | | (4.9) |
| *2011 - 2013* | 17431 | (53.4) | 702 | (56.9) | 4643 | (52.6) | 4113 | (52.1) | 2442 | (53) | 1090 | (52.6) | 870 | (53.8) | 13860 | | (52.8) | 3571 | | (55.8) |
| *2014 - 2015* | 13600 | (41.6) | 466 | (37.8) | 3736 | (42.3) | 3390 | (42.9) | 1942 | (42.2) | 876 | (42.3) | 673 | (41.6) | 11083 | | (42.2) | 2517 | | (39.3) |
| **Census Region, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  | |  |
| *Midwest* | 6259 | (19.2) | 242 | (19.6) | 1598 | (18.1) | 1450 | (18.4) | 861 | (18.7) | 460 | (22.2) | 396 | (24.5) | 5007 | | (19.1) | 1252 | | (19.6) |
| *Northeast* | 11445 | (35) | 361 | (29.3) | 2952 | (33.4) | 2762 | (35) | 1606 | (34.9) | 701 | (33.8) | 527 | (32.6) | 8909 | | (33.9) | 2536 | | (39.6) |
| *South* | 11383 | (34.8) | 498 | (40.4) | 3246 | (36.7) | 2760 | (34.9) | 1655 | (35.9) | 697 | (33.6) | 530 | (32.8) | 9386 | | (35.7) | 1997 | | (31.2) |
| *West* | 3576 | (10.9) | 133 | (10.8) | 1038 | (11.8) | 925 | (11.7) | 484 | (10.5) | 214 | (10.3) | 165 | (10.2) | 2959 | | (11.3) | 617 | | (9.6) |
| **Urban-rural setting, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  | |  |
| *Urban setting* | 23724 | (72.6) | 911 | (73.8) | 6357 | (72) | 5579 | (70.6) | 3394 | (73.7) | 1573 | (75.9) | 1262 | (78) | 19076 | | (72.6) | 4648 | | (72.6) |
| *Rural setting* | 8939 | (27.4) | 323 | (26.2) | 2477 | (28) | 2318 | (29.4) | 1212 | (26.3) | 499 | (24.1) | 356 | (22) | 7185 | | (27.4) | 1754 | | (27.4) |
| **Facility bed capacity, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  | |  |
| *< 100* | 3091 | (9.5) | 101 | (8.2) | 807 | (9.1) | 742 | (9.4) | 418 | (9.1) | 217 | (10.5) | 148 | (9.1) | 2433 | | (9.3) | 658 | | (10.3) |
| *100-199* | 3749 | (11.5) | 152 | (12.3) | 1102 | (12.5) | 967 | (12.2) | 531 | (11.5) | 221 | (10.7) | 166 | (10.3) | 3139 | | (12) | 610 | | (9.5) |
| *200-299* | 6969 | (21.3) | 286 | (23.2) | 1923 | (21.8) | 1637 | (20.7) | 1017 | (22.1) | 457 | (22.1) | 368 | (22.7) | 5688 | | (21.7) | 1281 | | (20) |
| *300-499* | 9971 | (30.5) | 392 | (31.8) | 2759 | (31.2) | 2439 | (30.9) | 1424 | (30.9) | 650 | (31.4) | 549 | (33.9) | 8213 | | (31.3) | 1758 | | (27.5) |
| *500+* | 8883 | (27.2) | 303 | (24.6) | 2243 | (25.4) | 2112 | (26.7) | 1216 | (26.4) | 527 | (25.4) | 387 | (23.9) | 6788 | | (25.8) | 2095 | | (32.7) |
| **Type of facility, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  | |  |
| *Teaching* | 24662 | (75.8) | 940 | (76.2) | 6596 | (74.7) | 5859 | (74.2) | 3441 | (74.7) | 1577 | (76.1) | 1248 | (77.1) | 19661 | | (74.9) | 5001 | | (79.8) |
| *Non-teaching* | 7867 | (24.2) | 294 | (23.8) | 2238 | (25.3) | 2038 | (25.8) | 1165 | (25.3) | 495 | (23.9) | 370 | (22.9) | 6600 | | (25.1) | 1267 | | (20.2) |
| **Volume of GI bleeder admissions at facility, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  | |  |
| *Low* | 8228 | (25.2) | 315 | (25.5) | 2090 | (23.7) | 1926 | (24.4) | 1168 | (25.4) | 546 | (26.4) | 386 | (23.9) | 6431 | | (24.5) | 1797 | | (28.1) |
| *Medium* | 11513 | (35.2) | 410 | (33.2) | 3172 | (35.9) | 2790 | (35.3) | 1644 | (35.7) | 685 | (33.1) | 578 | (35.7) | 9279 | | (35.3) | 2234 | | (34.9) |
| *High* | 12922 | (39.6) | 509 | (41.2) | 3572 | (40.4) | 3181 | (40.3) | 1794 | (38.9) | 841 | (40.6) | 654 | (40.4) | 10551 | | (40.2) | 2371 | | (37) |
| **SOFA score at admission, median (IQR)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  | |  |
| *SOFA Renal* | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) | 0 | | (0-1) | 0 | | (0-1) |
| *SOFA hepatic* | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | | (0-0) | 0 | | (0-0) |
| *SOFA Coag* | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | | (0-0) | 0 | | (0-0) |
| *SOFA cardiovascular* | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) | 0 | (0-1) | 0 | | (0-1) | 0 | | (0-1) |
| *SOFA GCS* | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | | (0-0) | 0 | | (0-0) |
| *SOFA pulm* | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | (0-0) | 0 | | (0-0) | 0 | | (0-0) |
| *SOFA Total* | 1 | (0-3) | 1 | (0-3) | 1 | (0-3) | 1 | (0-2) | 1 | (0-2) | 1 | (0-2) | 1 | (0-2) | 1 | | (0-2) | 1 | | (0-3) |
| **Elixhauser score, median (IQR)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  | |  |
|  | 3 | (2-5) | 4 | (2-5) | 3 | (2-5) | 3 | (2-5) | 3 | (2-5) | 3 | (2-5) | 4 | (2-5) | 3 | | (2-5) | 4 | | (2-5) |
| **Admitted to ICU, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  | |  |
| *Yes* | 4825 | (14.8) | 189 | (15.3) | 1329 | (15) | 1251 | (15.8) | 701 | (15.2) | 309 | (14.9) | 219 | (13.5) | 3998 | | (15.2) | 827 | | (12.9) |
| **ICU type, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  | |  |
| *Coronary/ Cardiac ICU* | 360 | (1.1) | 14 | (1.1) | 95 | (1.1) | 98 | (1.2) | 56 | (1.2) | 26 | (1.3) | 17 | (1.1) | 306 | | (1.2) | 54 | | (0.8) |
| *Medical ICU* | 651 | (2) | 21 | (1.7) | 180 | (2) | 161 | (2) | 104 | (2.3) | 42 | (2) | 36 | (2.2) | 544 | | (2.1) | 107 | | (1.7) |
| *Other/ Unspecified/ Neurology ICU* | 3510 | (10.7) | 140 | (11.3) | 991 | (11.2) | 920 | (11.6) | 499 | (10.8) | 212 | (10.2) | 148 | (9.1) | 2910 | | (11.1) | 600 | | (9.4) |
| *Surgical ICU* | 304 | (0.9) | 14 | (1.1) | 63 | (0.7) | 72 | (0.9) | 42 | (0.9) | 29 | (1.4) | 18 | (1.1) | 238 | | (0.9) | 66 | | (1) |
| *Not ICU* | 27838 | (85.2) | 1045 | (84.7) | 7505 | (85) | 6646 | (84.2) | 3905 | (84.8) | 1763 | (85.1) | 1399 | (86.5) | 22263 | | (84.8) | 5575 | | (87.1) |
| **ICU Length of Stay if in ICU, median (IQR)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  | |  |
|  | 5 | (4-8) | 6 | (4-9) | 6 | (4-8) | 5 | (4-8) | 5 | (4-8) | 5 | (4-8) | 5 | (4-8) | 5 | | (4-8) | 6 | | (4-8) |
| **Hospital Length of Stay, median (IQR)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  | |  |
|  | 4 | (3-7) | 5 | (4-8) | 5 | (3-7) | 4 | (3-7) | 4 | (3-6) | 4 | (3-6) | 5 | (3-7) | 4 | | (3-7) | 4 | | (3-6.8) |
| **In-Hospital death, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  | |  |
| *Yes* | 780 | (2.4) | 56 | (4.5) | 234 | (2.6) | 192 | (2.4) | 92 | (2) | 41 | (2) | 31 | (1.9) | 646 | | (2.5) | 134 | | (2.1) |
| **Discharge to hospice, n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  | |  |
| *Yes* | 600 | (1.8) | 66 | (5.3) | 231 | (2.6) | 126 | (1.6) | 55 | (1.2) | 21 | (1) | 20 | (1.2) | 519 | | (2) | 81 | | (1.3) |
| **Short-term mortality (death or hospice), n (%)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  | |  |
| *Yes* | 1380 | (4.2) | 122 | (9.9) | 465 | (5.3) | 318 | (4) | 147 | (3.2) | 62 | (3) | 51 | (3.2) | 1165 | | (4.4) | 215 | | (3.4) |
| Of 1,229,042 non-sepsis encounters, 34,291 gastrointestinal bleeds (GI bleeds) encounters requiring at least one blood transfusion and with available BMI data were identified  (578 Gastrointestinal hemorrhage; 578.0 Hematemesis; 578.1 Blood in stool; 578.9 Hemorrhage of gastrointestinal tract, unspecified).  Of these 34,291 encounters, any GI bleed enounters with sepsis, severe sepsis or septic shock were excluded based on the ICD-9-CM codes leaving 32,663 sepsis-free encounters. ICD-9-CM codes of sepsis included 038x septicemia; 995.91 sepsis; 995.92 severe sepsis; and 785.52 septic shock. For the GI bleed onset date, the date of first blood transfusion in the encounter was used (available in 11,362 encounters). When the date of blood transfusion was not available, we used the admission date.  Of these 32,663 GI Bleed encounters, data for 26,261 unique patients with all available data were identified. | | | | | | | | | | | | | | | | | | | | |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Table E7. Power calculation** | | | | | | | |
| **Scenario** | **BMI Category** | **Sepsis Sample Proportion** | **Mortality in sepsis sample** | **Unadjusted OR** | **Bivariate Proportion** | **Bivariate Required Sample Size \*** | **Sepsis Cohort Sample Size** |
|  |  |  |  |  |  |  |  |
| 1 | Underweight BMI *vs.* | 6.4% | 30.7% | 1.45 | 6.4/(6.4+33.0)=16.2% | 3366 | 3366/(0.064+0.33) => 8544 |
|  | Normal weight BMI | 33.0% | 23.7% |  | 33.0/(6.4+33.0)=83.8% |  |  |
| 2 | Overweight BMI *vs.* | 27.6% | 19.1% | 0.77 | 45.5% | 3755 | 3755/(0.276+0.33) => 6197 |
|  | Normal weight BMI | 33.0% | 23.7% |  | 54.5% |  |  |
| 3 | Obese Class I BMI *vs.* | 16.2% | 16.4% | 0.63 | 32.9% | 1624 | 1624/(0.162+0.33) => 3301 |
|  | Normal weight BMI | 33.0% | 23.7% |  | 67.1% |  |  |
| 4 | Obese Class II BMI *vs.* | 7.9% | 15.5% | 0.59 | 19.3% | 1831 | 1831/(0.079+0.33) => 4477 |
|  | Normal weight BMI | 33.0% | 23.7% |  | 80.7% |  |  |
| 5 | Obese Class III BMI *vs.* | 8.9% | 14.4% | 0.55 | 21.2% | 1303 | 1303/(0.089+0.33) => 3110 |
|  | Normal weight BMI | 33.0% | 23.7% |  | 78.8% |  |  |
| **\* Reference**  R Package powerMediation; Author Weiliang Qiu <stwxq@channing.harvard.edu>  https://cran.r-project.org/web/packages/powerMediation/powerMediation.pdf  Use function "SSizeLogisticBin": Calculating sample size for simple logistic regression with binary predictor; Author Weiliang Qiu <stwxq@channing.harvard.edu>  Usage: SSizeLogisticBin(p1, p2, B, alpha, power), where p1=P(mortality|X=0); p2=P(mortality|X=1); B=P(X=1); alpha=Type I error rate; power= power for testing if the odds ratio is equal to one.  Hsieh, FY, Bloch, DA, and Larsen, MD. A SIMPLE METHOD OF SAMPLE SIZE CALCULATION FOR LINEAR AND LOGISTIC REGRESSION. Statistics in Medicine. 1998; 17:1623- 1634.  Use X=0 for Normal weight BMI; X=1 for Otherwise; Significance level=0.01; and Power=0.8 | | | | | | | |